ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: November 11, 2011

ClinicalTrials.gov ID: NCT00903383

Study Identification

Unique Protocol ID:	Protocol LX3305.1-201-RA
Brief Title:	Study of LX3305 in Subjects With Active Rheumatoid Arthritis on Stable Methotrexate
Official Title:	A Phase 2, Multi-center, Randomized, Double Blind, Placebo-controlled, Multiple-dose Study to Determine the Safety and Efficacy of Daily Orally Administered LX3305 in Subjects With Active Rheumatoid Arthritis (RA) on Stable Methotrexate (MTX) Therapy
Secondary IDs:	LX3305.201, LX2931

Study Status

Record Verification:	November 2011
Overall Status:	Completed
Study Start:	July 2009 []
Primary Completion:	September 2010 [Actual]
Study Completion:	

Sponsor/Collaborators

Sponsor:	Lexicon Pharmaceuticals
Responsible Party:	Sponsor
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	

U.S. FDA-regulated Device:	
Unapproved/Uncleared Device:	No
U.S. FDA IND/IDE:	Yes
IND/IDE Information:	FDA Center: CDER IND/IDE Number: 75795 Serial Number: 0017 Has Expanded Access: No
Human Subjects Review:	Board Status: Approved Approval Number: 07/14/09 Board Name: Independent Investigational Review Board, Inc. Board Affiliation: United States: Food and Drug Administration Phone: 954-327-0778 Email: info@iirb.com Address: 6738 West Sunrise Blvd., Suite 102 Plantation, FL 33313
Data Monitoring:	No
FDA Regulated Intervention:	Yes
Section 801 Clinical Trial:	Yes

Study Description

Brief Summary:	The purpose of the study is to evaluate the safety, tolerability, and effectiveness of LX3305 versus a placebo control in subjects with active rheumatoid arthritis on stable methotrexate therapy.
Detailed Description:	

Conditions

Conditions:	Rheumatoid Arthritis
Keywords:	

Study Design

Study Type:	Interventional

Primary Purpose:	Treatment
Study Phase:	Phase 2
Interventional Study Model:	Parallel Assignment
Number of Arms:	4
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Allocation:	Randomized
Enrollment:	208 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Experimental: Low Dose A low dose of LX3305; daily oral intake for 12 weeks	Drug: LX3305 low dose A low dose of LX3305; daily oral intake for 12 weeks
Experimental: Mid Dose A mid dose of LX3305; daily oral intake for 12 weeks	Drug: LX3305 mid dose A mid dose of LX3305; daily oral intake for 12 weeks
Experimental: High Dose A high dose of LX3305; daily oral intake for 12 weeks	Drug: LX3305 high dose A high dose of LX3305; daily oral intake for 12 weeks
Placebo Comparator: Placebo Matching placebo dosing with daily oral intake for 12 weeks	Drug: Placebo Matching placebo dosing with daily oral intake for 12 weeks

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age:	18 Years
Maximum Age:	75 Years
Sex:	All
Gender Based:	
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

- Males and females aged 18-75 years old
- Rheumatoid arthritis present for at least 6 months, functional class I, II, or III as defined by ACR criteria
- Active disease as determined by the presence of ≥6 swollen joints, ≥6 tender joints, and serum C-reactive protein level > upper limit of normal

- Receiving stable dose of MTX (≥10 mg/wk) and folate supplementation at least 8 weeks prior to Day 1
- Ability to provide written informed consent

Exclusion Criteria:

- RA diagnosis prior to 16 years of age (Juvenile RA)
- Lack of response to >3 disease modifying anti-rheumatic drugs (DMARDs) or exposure to >1 biologic DMARD
- Use of DMARDs other than MTX within 12 weeks prior to Day 1
- Intra-articular and/or parenteral corticosteroids within 4 weeks prior to study Day 1
- Blood donation or receipt of live vaccine within 4 weeks prior to Day 1
- Major surgical procedure within 8 weeks prior to Day 1
- Any systemic inflammatory condition, recurrent infection, or current infection other than onychomycosis
- History of cancer within 5 years prior to Day 1
- Presence of hepatic or biliary disease
- History of tuberculosis
- History of human immunodeficiency virus (HIV)

Contacts/Locations

Central Contact Person: Barbara Brooks, Clinical Project Manager
Telephone: 281-863-3377

Central Contact Backup:

Study Officials: Joel P. Freiman, MD, MPH
Study Director
Lexicon Pharmaceuticals, Inc.

Locations: **United States, Texas**
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Bruntal, Czechia

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IPDSharing

Plan to Share IPD:

References

Citations:

Links:

Available IPD/Information:

Study Results

Participant Flow

Recruitment Details	There were 43 study centers in 6 countries (10 in the US, 8 in Bulgaria, 4 in Czech Republic, 7 in Hungary, 11 in Poland, and 3 in Serbia). The first subject was enrolled on 31 August 2009, and the last subject completed the study on 30 September 2010.
Pre-assignment Details	There was a 4 week screening period prior to the 12-week treatment period.

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Overall Study

	Low Dose	Mid Dose	High Dose	Placebo
Started	55	54	50	49

	Low Dose	Mid Dose	High Dose	Placebo
Completed	48	48	47	44
Not Completed	7	6	3	5
Adverse Event	1	2	3	1
Physician Decision	1	2	0	0
Lost to Follow-up	0	0	0	1
Decision of Sponsor	1	0	0	0
Withdrawal by Subject	4	1	0	2
Patient Decision - Lack of Efficacy	0	1	0	0
Patient Decision	0	0	0	1

Baseline Characteristics

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Baseline Measures

	Low Dose	Mid Dose	High Dose	Placebo	Total
Overall Number of Participants	55	54	50	49	208

		Low Dose	Mid Dose	High Dose	Placebo	Total
Age, Continuous Mean (Standard Deviation) Unit of measure: years	Number Analyzed	55 participants	54 participants	50 participants	49 participants	208 participants
		56.5 (9.25)	55.8 (9.20)	56.4 (10.89)	57.5 (10.19)	56.5 (9.83)
Sex: Female, Male Measure Type: Count of Participants Unit of measure: participants	Number Analyzed	55 participants	54 participants	50 participants	49 participants	208 participants
	Female	47 85.45%	43 79.63%	37 74%	41 83.67%	168 80.77%
	Male	8 14.55%	11 20.37%	13 26%	8 16.33%	40 19.23%

Outcome Measures

1. Primary Outcome Measure:

Measure Title	ACR20 Response at Week 12
Measure Description	Evaluates the efficacy of LX3305 by utilizing the American College of Rheumatology 20% response criteria (ACR20) at 12 weeks in subjects with active RA also receiving stable doses of MTX. For a response of ACR20, there had to be ≥20% improvement in swollen joint count, ≥20% improvement in painful/tender joint count, and ≥20% improvement in at least 3 of the following: subject's assessment of pain, global assessment of disease activity, assessment of physical function, or acute phase reactant (C-reactive protein or erythrocyte sedimentation rate).
Time Frame	Baseline and 12 weeks

Analysis Population Description
Intent to Treat Population

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Measured Values

	Low Dose	Mid Dose	High Dose	Placebo
Overall Number of Participants Analyzed	55	54	50	49
ACR20 Response at Week 12 Measure Type: Number Unit of measure: Participants	24	22	30	24

2. Secondary Outcome Measure:

Measure Title	ACR50 Response at Week 12
Measure Description	Evaluates the efficacy of LX3305 by utilizing the American College of Rheumatology 50% response criteria (ACR50) at 12 weeks in subjects with active RA also receiving stable doses of MTX. For a response of ACR50, there had to be ≥50% improvement in swollen joint count, ≥50% improvement in painful/tender joint count, and ≥50% improvement in at least 3 of the following: subject's assessment of pain, global assessment of disease activity, assessment of physical function, or acute phase reactant (C-reactive protein or erythrocyte sedimentation rate).
Time Frame	Baseline and 12 weeks

Analysis Population Description
Intent to Treat Population

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Measured Values

	Low Dose	Mid Dose	High Dose	Placebo
Overall Number of Participants Analyzed	55	54	50	49
ACR50 Response at Week 12 Measure Type: Number Unit of measure: Participants	6	5	11	12

3. Secondary Outcome Measure:

Measure Title	ACR70 Response at Week 12
Measure Description	Evaluates the efficacy of LX3305 by utilizing the American College of Rheumatology 70% response criteria (ACR70) at 12 weeks in subjects with active RA also receiving stable doses of MTX. For a response of ACR70, there had to be ≥70% improvement in swollen joint count, ≥70% improvement in painful/tender joint count, and ≥70% improvement in at least 3 of the following: subject's assessment of pain, global assessment of disease activity, assessment of physical function, or acute phase reactant (C-reactive protein or erythrocyte sedimentation rate).
Time Frame	Baseline and 12 weeks

Analysis Population Description
Intent to Treat Population

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Measured Values

	Low Dose	Mid Dose	High Dose	Placebo
Overall Number of Participants Analyzed	55	54	50	49
ACR70 Response at Week 12 Measure Type: Number Unit of measure: Participants	2	4	5	3

4. Secondary Outcome Measure:

Measure Title	Hybrid ACR Response at Week 12
Measure Description	Evaluates the improvement in active RA by combining elements of the ACR20/50/70 with a continuous score of the mean change in core set measures. The percentage improvement from baseline was computed in each of the components of the ACR. The average percent improvement was calculated and used with the subject's ACR20, ACR50, and ACR70 status to compute the hybrid ACR response, with a positive change indicating improvement.
Time Frame	Baseline and 12 weeks

Analysis Population Description
Intent to Treat Population

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Measured Values

	Low Dose	Mid Dose	High Dose	Placebo
Overall Number of Participants Analyzed	55	54	50	49
Hybrid ACR Response at Week 12 Mean (Standard Deviation) Unit of measure: Percent change	26.595 (23.2280)	27.422 (24.3453)	37.356 (26.1357)	35.290 (24.4368)

5. Secondary Outcome Measure:

Measure Title	Change From Baseline in C-reactive Protein (mg/L) at Week 12
Measure Description	The C-reactive protein value (mg/L) at baseline was subtracted from the value for each of the treatment groups at Week 12.
Time Frame	Baseline and 12 weeks

Analysis Population Description
Intent to Treat Population

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Measured Values

	Low Dose	Mid Dose	High Dose	Placebo
Overall Number of Participants Analyzed	55	54	50	49
Change From Baseline in C-reactive Protein (mg/L) at Week 12 Mean (Standard Deviation) Unit of measure: mg/L	-0.026 (15.7225)	5.342 (26.5937)	-5.316 (19.1959)	-7.983 (28.5387)

6. Secondary Outcome Measure:

Measure Title	Change From Baseline in Erythrocyte Sedimentation Rate (mm) at Week 12
Measure Description	The value for Erythrocyte Sedimentation Rate (mm) at baseline was subtracted from the value for each of the treatment groups at Week 12.
Time Frame	Baseline and 12 weeks

Analysis Population Description
Intent to Treat Population

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

Measured Values

	Low Dose	Mid Dose	High Dose	Placebo
Overall Number of Participants Analyzed	55	54	50	49
Change From Baseline in Erythrocyte Sedimentation Rate (mm) at Week 12 Mean (Standard Deviation) Unit of measure: mm	-2.5 (21.23)	-3.3 (20.23)	-9.7 (21.76)	-7.6 (18.05)

Reported Adverse Events

Time Frame	Adverse events were followed during the 12-week Treatment period and during the 30-day Follow-up period.
Adverse Event Reporting Description	[Not specified]

Reporting Groups

	Description
Low Dose	A low dose of LX3305; daily oral intake for 12 weeks
Mid Dose	A mid dose of LX3305; daily oral intake for 12 weeks
High Dose	A high dose of LX3305; daily oral intake for 12 weeks
Placebo	Matching placebo dosing with daily oral intake for 12 weeks

All-Cause Mortality

	Low Dose		Mid Dose		High Dose		Placebo	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total All-Cause Mortality	/		/		/		/	

Serious Adverse Events

	Low Dose		Mid Dose		High Dose		Placebo	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	2/55 (3.64%)		0/54 (0%)		0/50 (0%)		0/49 (0%)	
Cardiac disorders								
Atrial Fibrillation [A] †	1/55 (1.82%)	1	0/54 (0%)	0	0/50 (0%)	0	0/49 (0%)	0
Gastrointestinal disorders								
Nausea and Vomiting [A] †	1/55 (1.82%)	1	0/54 (0%)	0	0/50 (0%)	0	0/49 (0%)	0

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA (12.0)

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 5%

	Low Dose		Mid Dose		High Dose		Placebo	
	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events	Affected/ At Risk (%)	# Events
Total	10/55 (18.18%)		5/54 (9.26%)		10/50 (20%)		12/49 (24.49%)	
Gastrointestinal disorders								
Diarrhea [A] †	2/55 (3.64%)	2	3/54 (5.56%)	3	2/50 (4%)	3	1/49 (2.04%)	1
Infections and infestations								
Urinary Tract Infection [A] †	3/55 (5.45%)	4	1/54 (1.85%)	1	3/50 (6%)	5	6/49 (12.24%)	6
Musculoskeletal and connective tissue disorders								
Rheumatoid Arthritis [A] †	2/55 (3.64%)	2	1/54 (1.85%)	1	3/50 (6%)	3	2/49 (4.08%)	2
Nervous system disorders								
Headache [A] †	3/55 (5.45%)	3	0/54 (0%)	0	2/50 (4%)	2	3/49 (6.12%)	3

† Indicates events were collected by systematic assessment.

A Term from vocabulary, MedDRA (12.0)

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The sponsor requires that written permission be given before the PI can release any data publicly.

Results Point of Contact:

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