Results Registration Form

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Result Point of Contact

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Certain Agreements

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

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

The only disclosure restriction on the PI is that the sponsor can review results communications prior to public release and can embargo communications regarding trial results for a period that is more than 60 days but less than or equal to 180 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Participant Flow

Recruitment Details	This multicenter study was conducted in Europe, Asia, and North America between 4 February 2011 and 26 April 2012.
Pre-assignment Details	21-day screening/washout and 8-week prospective open-label SSRI(selective serotonin reuptake inhibitors)/SNRI(selective serotonin and norepinephrine reuptake inhibitors) periods to identify population of inadequate responders(<50% reduction in Hamilton Rating Scale for Depression total score of ≥16 and a Clinical Global Impression-Severity ≥4).

Period: Overall Study

	1 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	**4 mg BID TC-5214** NOTE: An entry in Arm/Group Description is recommended.	**60 mg QD Duloxetine** NOTE: An entry in Arm/Group Description is recommended.	**Placebo** NOTE: An entry in Arm/Group Description is recommended.	**Total** *(=sum per row)*
Started	37	36	37	35	145 *(calculated)*
Completed	17	9	18	18	62 *(calculated)*
Not Completed: *(=Started - Completed)*	20 *(calculated)*	27 *(calculated)*	19 *(calculated)*	17 *(calculated)*	83 *(calculated)*
Reason for Not Completed					
Total: *(=sum per column)*	20 *(calculated)*	27 *(calculated)*	19 *(calculated)*	17 *(calculated)*	83 *(calculated)*
Withdrawal by Subject	2	4	1	0	7 *(calculated)*
Adverse Event	2	1	2	3	8 *(calculated)*
Other Severe Non-Compliance to Protocol	1	3	1	3	8 *(calculated)*
Other Condition under Investigation Worsened	0	0	0	1	1 *(calculated)*
Lack of Efficacy	2	2	0	2	6 *(calculated)*
Other Study-Specific Withdrawal Criteria	1	1	0	0	2 *(calculated)*
Lost to Follow-up	1	1	1	0	3 *(calculated)*
Other Other or Study Termination	11	15	14	8	48 *(calculated)*

Baseline Characteristics

Overall Number of Baseline Participants

	1 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	**4 mg BID TC-5214** NOTE: An entry in Arm/Group Description is recommended.	**60 mg QD Duloxetine** NOTE: An entry in Arm/Group Description is recommended.	**Placebo** NOTE: An entry in Arm/Group Description is recommended.	**Total(=sum across Arm/Groups)**
Overall Number of Baseline Participants	37	36	37	35	145 *(calculated)*
Baseline Analysis Population Description					

Age Continuous (Units: years)

Mean
Standard Deviation

	1 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	**4 mg BID TC-5214** NOTE: An entry in Arm/Group Description is recommended.	**60 mg QD Duloxetine** NOTE: An entry in Arm/Group Description is recommended.	**Placebo** NOTE: An entry in Arm/Group Description is recommended.	**Total**

	44.5 (13.03)	40.3 (12.50)	41.8 (12.70)	40.1 (10.49)	41.7 (12.24)

Gender, Male/Female (Units: participants)

Number
Not Applicable

	1 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	4 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	60 mg QD Duloxetine NOTE: An entry in Arm/Group Description is recommended.	Placebo NOTE: An entry in Arm/Group Description is recommended.	Total *(=sum per row)*
Female	24	26	22	19	91 *(calculated)*
Male	13	10	15	16	54 *(calculated)*

Race/Ethnicity, Customized (Units: participants)

Number
Not Applicable

	1 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	4 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	60 mg QD Duloxetine NOTE: An entry in Arm/Group Description is recommended.	Placebo NOTE: An entry in Arm/Group Description is recommended.	Total *(=sum per row)*
White	23	20	23	20	86 *(calculated)*
Black or African American	1	4	4	5	14 *(calculated)*
Asian	12	10	9	9	40 *(calculated)*
Native Hawaiian or other Pacific Islander	0	0	0	0	0 *(calculated)*
American Indian or Alaska Native	0	0	0	0	0 *(calculated)*
Other	1	2	1	1	5 *(calculated)*

Study Specific Characteristic [Hamilton Rating Scale for Depression-17 items (HAMD-17) total score at randomization] (Units: Scores on a scale)
A 17-item, clinician-rated scale that assesses depressive symptoms. The Hamilton Rating Scale for Depression-17 items (HAMD-17) consists of 17 symptoms, each of which is rated from 0 to 2 or 0 to 4, where 0 is none/absent. Higher HAMD-17 scores indicate more severe depression.
Mean
Standard Deviation

	1 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	4 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	60 mg QD Duloxetine NOTE: An entry in Arm/Group Description is recommended.	Placebo NOTE: An entry in Arm/Group Description is recommended.	Total
	20.914 (3.425)	21.371 (3.606)	21.857 (3.499)	21.344 (4.100)	21.372 (3.632)

Study Specific Characteristic [Montgomery-Asberg Depression Rating Scale (MADRS) total score at randomization] (Units: Scores on a scale)
A 10-item scale for the evaluation of depressive symptoms. Each Montgomery-Asberg Depression Rating Scale (MADRS) item is rated on a 0 to 6 scale. The MADRS total score is calculated as the sum of the 10 individual item scores; the total score can range from 0 to 60. Higher MADRS scores indicate higher levels of depressive symptoms.
Mean
Standard Deviation

	1 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	4 mg BID TC-5214 NOTE: An entry in Arm/Group Description is recommended.	60 mg QD Duloxetine NOTE: An entry in Arm/Group Description is recommended.	Placebo NOTE: An entry in Arm/Group Description is recommended.	Total
	27.228 (5.202)	26.857 (5.542)	28.600 (6.796)	27.625 (5.320)	27.577 (5.734)

Outcome Measures

Expand All

1. Primary: Change in the Montgomery Asberg Depression Rating Scale (MADRS) Total Score from Randomization to End of Treatment

Description: A 10-item scale for the evaluation of depressive symptoms. Each Montgomery Asberg Depression Rating Scale (MADRS) item is rated on a 0 to 6 scale. The MADRS total score is calculated as the sum of the 10 individual item scores; the total score can range from 0 to 60. Higher MADRS scores indicate higher levels of depressive symptoms.

Time Frame: Randomization (Week 8) to end of treatment (Week 16)

Safety Issue: No

Analysis Population Description: Modified intent-to-treat analysis set including all randomized patients who received at least 1 dose of investigational product (TC-5214, duloxetine or placebo) and who had a randomization and at least 1 post-randomization MADRS total score.

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Number of Participants Analyzed:	35		35		35		32	
Change in the Montgomery Asberg Depression Rating Scale (MADRS) Total Score from Randomization to End of Treatment Units: units on a scale	Least Squares Mean	Standard Error	Least Squares Mean	Standard Error	Least Squares Mean	Standard Error	Least Squares Mean	Standard Error
	-9.1	2.15	-11.2	2.56	-11.4	2.14	-7.6	2.19

Statistical Analysis		
Groups	1 mg BID TC-5214, Placebo	Mixed model repeated measures (MMRM) includes treatment, pooled center, visit, treatment by visit interaction, region, responsiveness, and region by responsiveness as explanatory variables and the randomization MADRS total score as a covariate. Treatment, visit

		treatment by visit interaction, region, responsiveness, and region by responsiveness are fixed effects in the model; pooled center is a random effect.
Non-Inferiority/Equivalence Test	No	
P Value	0.617	
Method	Other MMRM	
Other LS mean	-1.5	
Standard Error of the mean	2.95	
95% Confidence Interval 2-Sided	-7.35 to 4.39	

Statistical Analysis		
Groups	4 mg BID TC-5214, Placebo	Mixed model repeated measures (MMRM) includes treatment, pooled center, visit, treatment by visit interaction, region, responsiveness, and region by responsiveness as explanatory variables and the randomization MADRS total score as a covariate. Treatment, visit, treatment by visit interaction, region, responsiveness, and region by responsiveness are fixed effects in the model; pooled center is a random effect.
Non-Inferiority/Equivalence Test	No	
P Value	0.277	
Method	Other MMRM	
Other LS mean	-3.6	
Standard Error of the mean	3.26	
95% Confidence Interval 2-Sided	-10.06 to 2.91	

Statistical Analysis		
Groups	60 mg QD Duloxetine, Placebo	Mixed model repeated measures (MMRM) includes treatment, pooled center, visit, treatment by visit interaction, region, responsiveness, and region by responsiveness as explanatory variables and the randomization MADRS total score as a covariate. Treatment, visit, treatment by visit interaction, region, responsiveness, and region by responsiveness are fixed effects in the model; pooled center is a random effect.
Non-Inferiority/Equivalence Test	No	
P Value	0.194	
Method	Other MMRM	
Other LS mean	-3.9	
Standard Error of the mean	2.95	
95% Confidence Interval 2-Sided	-9.72 to 2.00	

NOTE: An entry in Arm/Group Description is recommended. **[4 occurrences]**

Limitations and Caveats

The study was terminated early and thus only a fraction of the planned number of patients were randomized and many did not complete the study. As a consequence the possibility of interpreting efficacy over an 8 week period is considerably reduced.

Adverse Events

View Adverse Events