ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 04/23/2012

ClinicalTrials.gov ID: NCT00789854

Study Identification

Unique Protocol ID:	D1443L00044
Brief Title:	Comparing Quetiapine XR Monotherapy and Augmentation With Lithium Augmentation in TRD Patients (RUBY)
Official Title:	A Randomised, 6-week, Multicentre, Open-label, Rater-blinded Parallel Group Study Comparing Quetiapine Extended Release Monotherapy and Augmentation With Lithium Augmentation in Patients With Treatment Resistant Depression
Secondary IDs:	

Study Status

Record Verification:	April 2012
Overall Status:	Completed
Study Start:	November 2008
Primary Completion:	August 2009 [Actual]
Study Completion:	August 2009 [Actual]

Sponsor/Collaborators

Sponsor:	AstraZeneca
Responsible Party:	Sponsor
Collaborators:	

Oversight

FDA Regulated?:	Yes
Applicable Trial?:	Section 801 Clinical Trial? Yes

	Delayed Posting? No
IND/IDE Protocol?:	No
Review Board:	Approval Status: Approved Approval Number: 2008-000908-91 Board Name: AGES PharmMed Board Affiliation: Agency for Health and Food Agency, Austria Phone: +43 (0) 5 0555 36823 Email:
Data Monitoring?:	No
Plan to Share Data?:	
Oversight Authorities:	Australia: National Health and Medical Research Council Austria: Agency for Health and Food Safety Belgium: Federal Agency for Medicinal Products and Health Products Bulgaria: Bulgarian Drug Agency Denmark: Danish Medicines Agency Germany: Federal Institute for Drugs and Medical Devices Hungary: National Institute of Pharmacy Italy: The Italian Medicines Agency Portugal: National Pharmacy and Medicines Institute Romania: National Medicines Institute Slovakia: State Institute for Drug Control Spain: Spanish Agency of Medicines Sweden: Medical Products Agency United Kingdom: Medicines and Healthcare Products Regulatory Agency

Study Description

Brief Summary:	The primary objective of the study is to evaluate the efficacy of Quetiapine extended release (XR) in combination with an selective serotonin reuptake inhibitor (SSRI) or Venlafaxine versus Lithium in combination with an selective serotonin reuptake inhibitor or Venlafaxine versus Quetiapine extended release monotherapy in subjects with treatment resistant depression as assessed by the changes from randomisation to week 6 in the Montgomery-Åsberg Depression Rating Scale (MADRS) total score. As an independent objective, the primary objective will also be evaluated in two subgroups of patients: (1) patients who were resistant to two previous antidepressant therapies and (2) in the subgroup of patients with one previous failure.
Detailed Description:	The secondary objectives of the study are to compare the effects of the three different treatment regimen as assessed by the following variables and, if applicable, by their changes from randomisation to week 6 (end of study). Additionally the time of onset of therapeutic effect will be assessed by evaluating efficacy data after the first four days (Day 4) of treatment as well as after the first week of treatment (Day 8). These analyses will also be performed in the subgroups of patients with 2 failed previous antidepressants and patients with 1 failure.

Conditions

Conditions: Major Depressive Disorder
Treatment Resistant Depression

Keywords: Depression
MDD
TRD

Study Design

Study Type: Interventional
Primary Purpose: Treatment
Study Phase: Phase 3
Intervention Model: Parallel Assignment
Number of Arms: 3
Masking: Open Label
Allocation: Randomized
Endpoint Classification: Efficacy Study
Enrollment: 688 [Actual]

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Add-on Quetiapine XR+SSRI/Venlafaxine Selective serotonin reuptake inhibitors (SSRI) or Venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od). From previous anti-depressant treatment 64% of the patients had SSRI and 35% had Venlafaxine at baseline.	Drug: Quetiapine XR 300 mg once daily (od) Other Names: • Seroquel XR Drug: SSRI/Venlafaxine SSRI - doses within label, Venlafaxine dose up to 225 mg/day
Active Comparator: Add-on Lithium+SSRI/Venlafaxine Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od). From previous anti-depressant treatment 67% of the patients had SSRI and 33% had Venlafaxine at baseline.	Drug: Lithium carbonate 900 mg once daily (od) Other Names: • Quilonum Retard Drug: SSRI/Venlafaxine SSRI - doses within label, Venlafaxine dose up to 225 mg/day
Active Comparator: Monotherapy Quetiapine XR	Drug: Quetiapine XR

Arms	Assigned Interventions
Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)	300 mg once daily (od) Other Names: • Seroquel XR

Outcome Measures

[See Results Section.]

Eligibility

Minimum Age: 18 Years

Maximum Age: 65 Years

Gender: Both

Accepts Healthy Volunteers?: No

Criteria: Inclusion Criteria:

- Documented clinical diagnosis as confirmed by the M.I.N.I. meeting criteria from the Diagnostic and Statistical Manual of Mental disorders, 4th Edition (DSM-IV) for any of the following:296.2x MDD, Single Episode296.3x MDD, Recurrent Episode
- Current episode of depression present, at least 42 days prior to enrolment but not more than 18 months
- MADRS-Score ≥ 25 at enrolment and randomisation

Exclusion Criteria:

- Patients with a DSM-IV Axis I disorder other than MDD within 6 months of randomisation
- Patients with a diagnosis of DSM-IV Axis II disorder which has a major impact on the patient's current psychiatric status
- Patients who, in the investigator's judgment pose a current serious suicidal or homicidal risk, or have made a suicide attempt within the past 6 months

Contacts/Locations

Study Officials: Michael Bauer, professor
Study Principal Investigator
Germany

Birgit Ekholm, PhD
Study Director
AstraZeneca MC Sweden

Locations: Germany

Research Site
Aachen, Germany

United Kingdom
Research Site
Addlestone, Surrey, United Kingdom

Germany
Research Site
Augsburg, Germany

Portugal
Research Site
Braga, Portugal

Australia, Queensland
Research Site
Brisbane, Queensland, Australia

Italy
Research Site
Brunico, BZ, Italy

Romania
Research Site
Bucharest, Romania

Italy
Research Site
Cagliari, CA, Italy

Research Site
Catania, Italy

Germany
Research Site
Chemnitz, Germany

Australia, Victoria
Research Site
Clayton, Victoria, Australia

Portugal
Research Site
Coimbra, Portugal

United Kingdom
Research Site
Coventry, United Kingdom

Romania
Research Site
Craiova, Romania

Germany
Research Site
Erbach, Germany

Denmark
Research Site
Esbjerg N, Denmark

Australia, Queensland
Research Site
Everton Park, Queensland, Australia

Australia, Victoria
Research Site
Frankston, Victoria, Australia

Denmark
Research Site
Frederiksberg, Denmark

Romania
Research Site
Galati, Galati, Romania

Australia, Australian Capital Territory
Research Site
Garran, Australian Capital Territory, Australia

Australia, South Australia
Research Site
Gilberton, South Australia, Australia

United Kingdom
Research Site
Glasgow, United Kingdom

Germany
Research Site

Gutersloh, Germany

Hungary
Research Site
Gyula, Hungary

Germany
Research Site
Halle, Germany

United Kingdom
Research Site
Harrow, United Kingdom

Australia, Victoria
Research Site
Heidelberg, Victoria, Australia

United Kingdom
Research Site
Horsham, West Sussex, United Kingdom

Research Site
Hull, United Kingdom

Bulgaria
Research Site
Kardjali, Bulgaria

Germany
Research Site
Kassel, Germany

Austria
Research Site
Klagenfurt, Austria

Slovakia
Research Site
Krupina, Slovakia

Portugal
Research Site
Lisboa, Portugal

Australia, Victoria

Research Site
Malvern, Victoria, Australia

Italy
Research Site
Napoli, Italy

Germany
Research Site
Neu-isenburg, Germany

Research Site
Nurnberg, Germany

Hungary
Research Site
Nyiregyhaza, Hungary

Denmark
Research Site
Odense, Denmark

Bulgaria
Research Site
Pazardjik, Bulgaria

Italy
Research Site
Pisa, PI, Italy

Australia, Victoria
Research Site
Prahran, Victoria, Australia

Slovakia
Research Site
Presov, Slovakia

Australia, Victoria
Research Site
Richmond, Victoria, Australia

Italy
Research Site
Roma, RM, Italy

Research Site
Roma, Italy

Austria
Research Site
Salzburg, Austria

Portugal
Research Site
Santarem, Portugal

Bulgaria
Research Site
Sofia, Bulgaria

Germany
Research Site
Stuttgart, Germany

Bulgaria
Research Site
Varna, Bulgaria

Austria
Research Site
Wels, Austria

United Kingdom
Research Site
Winnick, Warrington, United Kingdom

Research Site
Winsford, United Kingdom

Slovakia
Research Site
Zlate Moravce, Slovakia

Germany
Research Site
Achim, Germany

Belgium
Research Site
Assebroek, Belgium, Belgium

Germany
Research Site
Bad Homburg, Germany

Research Site
Bad Honnef, Germany

Research Site
Bad Saarow, Germany

Spain
Research Site
Barcelona, Cataluna, Spain

Germany
Research Site
Berlin, Germany

Research Site
Bielefeld, Germany

Research Site
Bochum, Germany

Italy
Research Site
Bolzano, Italy

Slovakia
Research Site
Bratislava, Slovakia

Italy
Research Site
Bressanone, BZ, Italy

Hungary
Research Site
Budapest, Hungary

Germany
Research Site
Butzbach, Germany

Bulgaria
Research Site

Cerova Koria Village, Veliko Tarnovo, Bulgaria

Belgium
Research Site
Diest, Belgium, Belgium

Germany
Research Site
Dresden, Germany

Research Site
Duren, Germany

Research Site
Dusseldorf, Germany

Research Site
Ellwangen, Germany

Research Site
Gelsenkirchen, Germany

Austria
Research Site
Graz, Austria

Hungary
Research Site
Gyor, Hungary

Germany
Research Site
Hattingen, Germany

Research Site
Herborn, Germany

Research Site
Kothen, Germany

Slovakia
Research Site
Levice, Slovakia

Belgium
Research Site

Liege, Belgium, Belgium

Slovakia
Research Site
Liptovsky Mikulas, Slovakia

Research Site
Michalovce Stranany, Slovakia

Germany
Research Site
Neubrandenburg, Germany

Research Site
Oldenburg, Germany

Research Site
Ostfildern, Germany

Bulgaria
Research Site
Pleven, Bulgaria

Slovakia
Research Site
Roznava, Slovakia

Bulgaria
Research Site
Ruse, Bulgaria

Spain
Research Site
Salamanca, Castilla Leon, Spain

Research Site
Sama de Langreo, Asturias, Spain

Germany
Research Site
Schwerin, Germany

Romania
Research Site
Sibiu, Romania

Belgium
Research Site
Tielt, Belgium

Australia, Queensland
Research Site
Townsville, Queensland, Australia

Spain
Research Site
Vigo, Galicia, Spain

Germany
Research Site
Westerstede, Germany

Austria
Research Site
Wien, Austria

Germany
Research Site
Wurzburg, Germany

Spain
Research Site
Zamora, Castilla Leon, Spain

Slovakia
Research Site
Zilina-bytcica, Slovakia

Austria
Research Site
Wiener NEUSTADT, Austria

References

Citations:

Links:

Study Data/Documents:

Participant Flow

Recruitment Details	This was a 3 arm, open-label randomised, rater blinded, parallel group study comparing quetiapine XR monotherapy and augmentation with lithium augmentation in patients with treatment resistant depression, Recruitment period 6 November 2008 to 19 June 2009
Pre-Assignment Details	At visit 1 and 2 (randomisation) the patients should have a Montgomery-Asberg Depression Rating Scale (MADRS) total score above or equal to 25

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Overall Study

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Started	228	231	229
Completed	179	196	182
Not Completed	49	35	47
Adverse Event	28	23	18
Lost to Follow-up	1	1	4
Withdrawal by Subject	9	6	17
Eligibility criteria not fulfilled	2	5	1
Severe non-compliance to the protocol	3	0	0
Safety reasons	0	0	2
Unknown	6	0	5

Baseline Characteristics

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Baseline Measures

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium	Total
Number of Participants	225	229	221	675
Age, Continuous [1] [units: years] Mean (Full Range)	47 (20 to 65)	47 (20 to 67)	47 (19 to 67)	47 (19 to 67)
Gender, Male/Female [1] [units: Participants]				
Female	152	162	152	466
Male	73	67	69	209
Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) [units: Participants]				
Diagnose code 296.2x Major Depressive Disorder (MD	50	36	41	127
Diagnose code 296.3x MDD, Recurrent	175	193	180	548
Montgomery-Asberg Depression Rating Scale (MADRS) total score [2] [units: Units on a scale] Mean (Standard Deviation)	33.74 (5.6)	33.15 (5.34)	32.91 (5.2)	33.32 (5.4)

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium	Total
Weight [units: kg] Mean (Standard Deviation)	75.3 (17.2)	75.2 (17)	76.4 (16.1)	75.8 (16.65)

[1] Baseline characteristics are presented using the ITT population (Quetiapine XR mono 225 participants, Add-on Quetiapine XR 229 participants and Add-on Lithium 221 participants) and not all randomized patients

[2] Units on a scale from 0 to 60. Lower score indicates a better health status.

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Per Protocol Analysis Set)
Measure Description	Change in LS mean total Montgomery Asberg Depression Rating Scale (MADRS) score from randomisation to end-of-treatment (week 6) (Scale 0-60), lower score indicates a better health status.
Time Frame	6 weeks treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

Analysis was 'per protocol'. Exclusion reason from analysis: Violation of exclusion/inclusion criteria; Non-compliance regarding prohibited concomitant medication, Total unavailability of MADRS score after randomization, Patient not treated with any dose of study drug after randomization, Non-compliance regarding titration to 300 mg quetiapine/d.

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	180	183	109
Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Per Protocol Analysis Set) [units: scores on a scale] Least Squares Mean (Standard Error)	-16.2 (0.843)	-17.2 (0.826)	-14.9 (0.97)

Statistical Analysis 1 for Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Per Protocol Analysis Set)

Statistical Analysis Overview	Comparison Groups	Add-on Quetiapine XR, Add-on Lithium
	Comments	Add-on quetiapine XR was tested versus add-on lithium for non-inferiority. The null hypothesis was that the add-on quetiapine treatment was non-inferior to add-on lithium.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	The non-inferiority margin for differences was set to 3 units in the MADRS total score. A power set to 80% and using a Bonferroni-adjusted one-sided alpha* = alpha/3 = 0.0083 yields a planned sample size of 192 patients per study group. With a drop out of 4% a total of 600 randomized patients were required to obtain 192 efficacy evaluable patients per treatment group.

Statistical Test of Hypothesis	P-Value	
	Comments	The CI is for comparing add-on quetiapine versus add-on Lithium. The CI = confidence interval was adjusted for multiple comparisons. The -0.05 value should have been +3 or above to fail to reject the null hypothesis.
	Method	ANCOVA
	Comments	Non-inferiority between add-on quetiapine XR and add-on lithium was shown in the Per Protocol analysis set.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-2.322
	Confidence Interval	(2-Sided) 97.5% -4.6 to -0.05

	Estimation Comments	[Not specified]

Statistical Analysis 2 for Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Per Protocol Analysis Set)

Statistical Analysis Overview	Comparison Groups	Quetiapine XR Mono, Add-on Lithium
	Comments	Quetiapine XR mono was tested versus add-on lithium for non-inferiority. The null hypothesis was that the quetiapine XR mono treatment was non-inferior to add-on lithium.
	Non-Inferiority or Equivalence Analysis?	Yes
	Comments	The non-inferiority margin for differences was set to 3 units in the MADRS total score. A power set to 80% and using a Bonferroni-adjusted one-sided alpha* = alpha/3 = 0.0083 yields a planned sample size of 192 patients per study group. With a drop out of 4% a total of 600 randomized patients were required to obtain 192 efficacy evaluable patients per treatment group.

Statistical Test of Hypothesis	P-Value	
	Comments	The CI is for comparing quetiapine XR mono versus add-on Lithium. The CI = confidence interval was adjusted for multiple comparisons. The 1.312 value should have been +3 or above to fail to reject the null hypothesis.
	Method	ANCOVA
	Comments	Non-inferiority between quetiapine XR mono and add-on lithium was shown in the Per Protocol analysis set.

Method of Estimation	Estimation Parameter	Mean Difference (Final Values)
	Estimated Value	-1.639
	Confidence Interval	(2-Sided) 97.5% -3.24 to 1.312
	Estimation Comments	[Not specified]

2. Primary Outcome Measure:

Measure Title	Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Modified Intention to Treat Analysis Set)
Measure Description	Change in LS mean total Montgomery Asberg Depression Rating Scale (MADRS) score from randomisation to end-of-treatment (week 6) (Scale 0-60), lower score indicates a better health status.
Time Frame	6 weeks of treatment

Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	225	229	221
Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Modified Intention to Treat Analysis Set) [units: scores on a scale] Least Squares Mean (Standard Error)	-13.9 (0.806)	-15.1 (0.797)	-13.3 (0.801)

Statistical Analysis 1 for Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Modified Intention to Treat Analysis Set)

Statistical Analysis Overview	Comparison Groups	Add-on Quetiapine XR, Add-on Lithium
	Comments	The null hypothesis was that the add-on quetiapine XR treatment was not different to the add-on lithium treatment. The power calculation was done for the primary non-inferior analysis. This superiority analysis was only done if the non-inferior analysis was successful.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.0489
	Comments	Adjustment for multiplicity was done, alpha = 0.025
	Method	ANCOVA
	Comments	Superiority testing of primary outcome showed no significant difference in the Modified Intention To Treat (ITT) population

Statistical Analysis 2 for Change in Depressive Symptoms Between Randomisation and Week 6 Measured by Change in Montgomery Asberg Depression Rating Scale (MADRS) Total Score (Modified Intention to Treat Analysis Set)

Statistical Analysis Overview	Comparison Groups	Quetiapine XR Mono, Add-on Lithium
	Comments	The null hypothesis was that the quetiapine XR mono treatment was not different from the add-on lithium treatment. The power calculation was done for the primary non-inferior analysis. This superiority analysis was only done if the non-inferior analysis was successful.
	Non-Inferiority or Equivalence Analysis?	No
	Comments	[Not specified]

Statistical Test of Hypothesis	P-Value	0.4368
	Comments	Adjustment for multiplicity was done, alpha = 0.025
	Method	ANCOVA
	Comments	Superiority testing of primary outcome showed no significant difference in the Modified Intention To Treat (ITT) population

3. Secondary Outcome Measure:

Measure Title	Depression Remission; Montgomery-Asberg Depression Rating Scale MADRS ≤10, All Patients
Measure Description	Number of patients in remission, with total Montgomery Asberg Depression Rating Scale (MADRS) score ≤10. MADRS scale has range from 0 to 60, where the lower score indicates the better health status.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	225	229	221
Depression Remission; Montgomery-Asberg Depression Rating Scale MADRS ≤10, All Patients [units: Participants]	53	73	60

4. Secondary Outcome Measure:

Measure Title	Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤10, Patients With One Previous Treatment Failure
Measure Description	Number of patients in remission with one previous treatment failure and with total Montgomery Asberg Depression Rating Scale (MADRS) score ≤10. MADRS scale has range from 0 to 60, where the lower score indicates the better health status.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)

	Description
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	114	117	114
Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤10, Patients With One Previous Treatment Failure [units: Participants]	22	42	31

5. Secondary Outcome Measure:

Measure Title	Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤10, Patients With Two Previous Treatment Failure
Measure Description	Number of patients in remission with two previous treatment failure and with total Montgomery Asberg Depression Rating Scale (MADRS) score ≤10. MADRS scale has range from 0 to 60, where the lower score indicates the better health status.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)

	Description
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	114	114	115
Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤10, Patients With Two Previous Treatment Failure [units: Participants]	31	31	29

6. Secondary Outcome Measure:

Measure Title	Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤8
Measure Description	Number of patients in remission with total Montgomery Asberg Depression Rating Scale (MADRS) score ≤8. MADRS scale has range from 0 to 60, where the lower score indicates the better health status.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	225	229	221
Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤8 [units: Participants]	35	58	45

7. Secondary Outcome Measure:

Measure Title	Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤12
Measure Description	Number of patients in remission with total Montgomery Asberg Depression Rating Scale (MADRS) score ≤12. MADRS scale has range from 0 to 60, where the lower score indicates the better health status.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	225	229	221
Depression Remission; Montgomery-Asberg Depression Rating Scale (MADRS) ≤12 [units: Participants]	67	89	73

8. Secondary Outcome Measure:

Measure Title	Response Rate; Montgomery-Asberg Depression Rating Scale (MADRS) Score Reduced ≥ 50%, All Patients
Measure Description	Response rate at end of study measured as number of patients with Montgomery Asberg Depression Rating Scale (MADRS) with total score reduction ≥ 50% compared to baseline, the higher number of patients the better
Time Frame	6 week of treatments
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	225	229	221
Response Rate; Montgomery-Asberg Depression Rating Scale (MADRS) Score Reduced ≥ 50%, All Patients [units: Participants]	114	120	102

9. Secondary Outcome Measure:

Measure Title	Response Rate; Montgomery-Asberg Depression Rating Scale (MADRS) Score Reduced ≥ 50%, Patients With One Previous Treatment Failure

Measure Description	Response rate at end of study measured as number of patients with Montgomery Asberg Depression Rating Scale (MADRS) with total score reduction ≥ 50% compared to baseline, the higher number of patients the better
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	114	117	114
Response Rate; Montgomery-Asberg Depression Rating Scale (MADRS) Score Reduced ≥ 50%, Patients With One Previous Treatment Failure [units: Participants]	54	65	53

10. Secondary Outcome Measure:

Measure Title	Response Rate; Montgomery-Asberg Depression Rating Scale (MADRS) Score Reduced ≥ 50%, Patients With Two Previous Treatment Failure
Measure Description	Response rate at end of study measured as number of patients with Montgomery Asberg Depression Rating Scale (MADRS) with total score reduction ≥ 50% compared to baseline, the higher number of patients the better
Time Frame	6 weeks of treatment
Safety Issue?	No

Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	114	114	115
Response Rate; Montgomery-Asberg Depression Rating Scale (MADRS) Score Reduced ≥ 50%, Patients With Two Previous Treatment Failure [units: Participants]	60	55	49

11. Secondary Outcome Measure:

Measure Title	Responder: Clinical Global Impression Improvement (CGI-I) Item 2, All Patients
Measure Description	Change in global improvement measured by Clinical Global Impression Improvement (CGI-I). Scale from 1-4, where lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	224	229	220
Responder: Clinical Global Impression Improvement (CGI-I) Item 2, All Patients [units: scores on a scale] Mean (Standard Deviation)	-1.54 (1.24)	-1.85 (1.34)	-1.58 (1.32)

12. Secondary Outcome Measure:

Measure Title	Responder: Clinical Global Impression Improvement (CGI)-I Item 2, Patients With One Previous Treatment Failure
Measure Description	Change in global improvement measured by Clinical Global Impression Improvement (CGI-I). Scale from 1-4, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)

	Description
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	113	115	111
Responder: Clinical Global Impression Improvement (CGI)-I Item 2, Patients With One Previous Treatment Failure [units: scores on a scale] Mean (Standard Deviation)	-1.42 (1.17)	-1.91 (1.31)	-1.62 (1.27)

13. Secondary Outcome Measure:

Measure Title	Responder: Clinical Global Impression Improvement (CGI-I) Item 2, Patients With Two Previous Treatment Failure
Measure Description	Change in global improvement measured by Clinical Global Impression Improvement (CGI-I). Scale from 1-4, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	111	114	109
Responder: Clinical Global Impression Improvement (CGI-I) Item 2, Patients With Two Previous Treatment Failure [units: scores on a scale] Mean (Standard Deviation)	-1.67 (1.30)	-1.79 (1.36)	-1.54 (1.38)

14. Secondary Outcome Measure:

Measure Title	Change in Clinical Global Impression Scale (CGI-S), All Patients
Measure Description	Change in severity of illness measured by Clinical Global Impression Scale (CGI-S). Scale form 1-7, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	224	229	220
Change in Clinical Global Impression Scale (CGI-S), All Patients [units: scores on a scale]	-1.43 (0.101)	-1.65 (0.099)	-1.49 (0.1)

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Least Squares Mean (Standard Error)			

15. Secondary Outcome Measure:

Measure Title	Change in Clinical Global Impression Scale (CGI-S), Patients With One Previous Treatment Failure
Measure Description	Change in severity of illness measured by Clinical Global Impression Scale (CGI-S). Scale from 1-7, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	113	115	111
Change in Clinical Global Impression Scale (CGI-S), Patients With One Previous Treatment Failure [units: scores on a scale] Least Squares Mean (Standard Error)	-1.45 (0.133)	-1.82 (0.13)	-1.59 (0.13)

16. Secondary Outcome Measure:

Measure Title	Change in Clinical Global Impression Scale (CGI-S), Patients With Two Previous Treatment Failure
Measure Description	Change in severity of illness measured by Clinical Global Impression Scale (CGI-S). Scale from 1-7, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	111	114	109
Change in Clinical Global Impression Scale (CGI-S), Patients With Two Previous Treatment Failure [units: scores on a scale] Least Squares Mean (Standard Error)	-1.52 (0.133)	-1.55 (0.131)	-1.45 (0.135)

17. Secondary Outcome Measure:

Measure Title	Change in Beck Depression Inventory (BDI)
Measure Description	Self-rating assessment of depressive symptoms using Beck Depression Inventory (BDI). Scale from 0-63, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment

Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	213	212	205
Change in Beck Depression Inventory (BDI) [units: scores on a scale] Least Squares Mean (Standard Error)	-11.7 (0.926)	-13.5 (0.921)	-12.2 (0.922)

18. Secondary Outcome Measure:

Measure Title	Change in Pain, Measured by Visual Analog Scale (VAS)
Measure Description	Self-rating assessment of pain using a visual analogue scale (VAS). Scale from 0-100, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	221	222	218
Change in Pain, Measured by Visual Analog Scale (VAS) [units: scores on a scale] Least Squares Mean (Standard Error)	-9.47 (1.695)	-8.03 (1.681)	-8.3 (1.682)

19. Secondary Outcome Measure:

Measure Title	Change in Anxiety Measured by Visual Analog Scale (VAS)
Measure Description	Self-rating assessment of anxiety using a visual analogue scale (VAS). Scale from 0-100, where a lower value shows a larger improvement.
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)

	Description
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	219	224	218
Change in Anxiety Measured by Visual Analog Scale (VAS) [units: scores on a scale] Least Squares Mean (Standard Error)	-21.2 (1.972)	-23.4 (1.947)	-20.6 (1.952)

20. Secondary Outcome Measure:

Measure Title	Change in Anxiety Measured by State-Trait Anxiety Inventory (STAI), State Anxiety Inventory
Measure Description	Self-rating assessment of anxiety measured by STAI, state anxiety inventory (Scale 20-80, where a lower value shows a larger improvement)
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	223	227	217
Change in Anxiety Measured by State-Trait Anxiety Inventory (STAI), State Anxiety Inventory [units: Scores on a scale] Least Squares Mean (Standard Error)	-0.62 (0.347)	0.014 (0.344)	-0.87 (0.35)

21. Secondary Outcome Measure:

Measure Title	Change in Anxiety Measured by STAI, Trait Anxiety Inventory
Measure Description	Self-rating assessment of anxiety measured by State-Trait Anxiety Inventory (STAI), trait anxiety inventory (Scale 20-80, where a lower value shows a larger improvement)
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	220	220	214
Change in Anxiety Measured by STAI, Trait Anxiety Inventory [units: Scores on a scale]	-1.01 (0.331)	-1.36 (0.328)	-1.39 (0.331)

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Least Squares Mean (Standard Error)			

22. Secondary Outcome Measure:

Measure Title	Change in Sleep Quality Measured by Montgomery Asberg Depression Rating Scale (MADRS), Item 4
Measure Description	Sleeping quality measured by Montgomery-Asberg Depression Rating Scale (MADRS) item 4 (reduced sleep) (Scale 0-6, where a lower value shows a larger improvement)
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	225	229	221
Change in Sleep Quality Measured by Montgomery Asberg Depression Rating Scale (MADRS), Item 4 [units: MADRS item 4 score] Least Squares Mean (Standard Error)	-2.2 (0.108)	-2.4 (0.107)	-1.63 (0.108)

23. Secondary Outcome Measure:

Measure Title	Change in Sleep Quality Measured by Pittsburgh Sleep Quality Index (PSQI)
Measure Description	Self-rated sleeping quality measured by PSQI (Scale 0-21, subscales 0-3, 18 questions, where a lower value shows a larger improvement)
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	200	196	185
Change in Sleep Quality Measured by Pittsburgh Sleep Quality Index (PSQI) [units: Scores on a scale] Least Squares Mean (Standard Error)	-4.77 (0.36)	-4.96 (0.358)	-3.51 (0.364)

24. Secondary Outcome Measure:

Measure Title	Change in Quality of Life Measured by Short-form Health Survey (SF-36), Mental Component
Measure Description	Self rating assessment of quality in life using SF-36, mental component (Scale 0-100, where a higher value shows a larger improvement)
Time Frame	6 weeks of treatment

Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	178	171	174
Change in Quality of Life Measured by Short-form Health Survey (SF-36), Mental Component [units: Scores on a scale] Least Squares Mean (Standard Error)	9.59 (0.929)	10.77 (0.925)	9.66 (0.932)

25. Secondary Outcome Measure:

Measure Title	Change in Quality of Life Measured by Short-form Health Survey (SF-36), Physical Component
Measure Description	Self rating assessment of quality in life using SF-36, physical component (Scale 0-100, where a higher value shows a larger improvement)
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	178	171	174
Change in Quality of Life Measured by Short-form Health Survey (SF-36), Physical Component [units: Scores on a scale] Least Squares Mean (Standard Error)	5.224 (0.811)	5.065 (0.813)	4.566 (0.817)

26. Secondary Outcome Measure:

Measure Title	Change in Quality of Life Measured by Health Questionnaire EQ-5D as Utility
Measure Description	Self rating assessment of quality in life using EQ-5D utility (Scale 0-100, where a higher value shows a larger improvement)
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)

	Description
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	220	220	215
Change in Quality of Life Measured by Health Questionnaire EQ-5D as Utility [units: Scores on a scale] Least Squares Mean (Standard Error)	0.184 (0.023)	0.224 (0.023)	0.208 (0.023)

27. Secondary Outcome Measure:

Measure Title	Change in Work Productivity and Activity Impairment: General Health (WPAI:GH)
Measure Description	Self rating assessment of working productivity using WPAI:GH (Scale 0 to number of hours worked during a week multiplied with the salary in Euro, a lower value shows a larger improvement)
Time Frame	6 weeks of treatment
Safety Issue?	No
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	31	39	25
Change in Work Productivity and Activity Impairment: General Health (WPAI:GH) [units: Scores on a scale] Least Squares Mean (Standard Error)	-233 (0.023)	-185 (0.023)	-299 (0.023)

28. Secondary Outcome Measure:

Measure Title	Change in Clinical Global Impression (CGI) Item 4 Efficacy and Safety Combined, All Patients
Measure Description	The physician has evaluated the therapeutic effect and the side effect combined at end of study. Patients with a 'marked/moderate' therapeutic effect and 'None/Do Not Significantly Interfere' side effect has been added. The higher values show more patients with a treatment effect without any side-effect. The range is from 0 patients to the maximum number of patients in the treatment arm (225, 229 or 221).
Time Frame	6 weeks of treatment
Safety Issue?	Yes
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	225	229	221

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Change in Clinical Global Impression (CGI) Item 4 Efficacy and Safety Combined, All Patients [units: Participants]	135	146	131

29. Secondary Outcome Measure:

Measure Title	Change in Clinical Global Impression (CGI) Item 4 Efficacy and Safety Combined, Patients With One Previous Treatment Failure
Measure Description	The physician has evaluated the therapeutic effect and the side effect combined at end of study. Patients with a 'marked/moderate' therapeutic effect and 'None/Do Not Significantly Interfere' side effect has been added. The higher values show more patients with a treatment effect without any side-effect. The range is from 0 patients to the maximum number of patients in the treatment arm.
Time Frame	6 weeks of treatment
Safety Issue?	Yes
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	113	115	111
Change in Clinical Global Impression (CGI) Item 4 Efficacy and Safety Combined, Patients With One Previous Treatment Failure [units: Participants]	67	75	69

30. Secondary Outcome Measure:

Measure Title	Change in Clinical Global Impression (CGI) Item 4 Efficacy and Safety Combined, Patients With Two Previous Treatment Failures
Measure Description	The physician has evaluated the therapeutic effect and the side effect combined at end of study. Patients with a 'marked/moderate' therapeutic effect and 'None/Do Not Significantly Interfere' side effect has been added. The higher values show more patients with a treatment effect without any side-effect. The range is from 0 patients to the maximum number of patients in the treatment arm.
Time Frame	6 week of treatments
Safety Issue?	Yes
Anticipated Reporting Date	August 2010

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Measured Values

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
Number of Participants Analyzed	112	114	110
Change in Clinical Global Impression (CGI) Item 4 Efficacy and Safety Combined, Patients With Two Previous Treatment Failures [units: Participants]	68	71	62

Reported Adverse Events

Time Frame	[Not specified]
Additional Description	[Not specified]

Reporting Groups

	Description
Quetiapine XR Mono	Switch from previous treatment with SSRI or venlafaxine to quetiapine XR monotherapy, 300mg tablet once daily (od)
Add-on Quetiapine XR	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with quetiapine XR, 300mg tablet once daily (od)
Add-on Lithium	Selective serotonin reuptake inhibitors (SSRI) or venlafaxine from previous therapy + add-on treatment with lithium, approximately 900mg tablet once daily (od)

Serious Adverse Events

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	5/228 (2.19%)	5/231 (2.16%)	2/229 (0.87%)
Gastrointestinal disorders			
Diarrhoea [A] †	0/228 (0%)	1/231 (0.43%)	0/229 (0%)
Hepatobiliary disorders			
Cholelithiasis [A] †	0/228 (0%)	0/231 (0%)	1/229 (0.44%)
Injury, poisoning and procedural complications			
Overdose [A] †	1/228 (0.44%)	0/231 (0%)	0/229 (0%)
Psychiatric disorders			
Affective Disorder [A] †	1/228 (0.44%)	0/231 (0%)	0/229 (0%)
Depression [A] †	0/228 (0%)	3/231 (1.3%)	1/229 (0.44%)
Mania [A] †	0/228 (0%)	1/231 (0.43%)	0/229 (0%)
Psychotic Disorder [A] †	1/228 (0.44%)	0/231 (0%)	0/229 (0%)
Restlessness [A] †	1/228 (0.44%)	0/231 (0%)	0/229 (0%)

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Suicidal Ideation [A] †	1/228 (0.44%)	0/231 (0%)	0/229 (0%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.0)

Other Adverse Events

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

	Quetiapine XR Mono	Add-on Quetiapine XR	Add-on Lithium
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	93/228 (40.79%)	90/231 (38.96%)	41/229 (17.9%)
Gastrointestinal disorders			
Dry mouth [A] †	13/228 (5.7%)	22/231 (9.52%)	6/229 (2.62%)
General disorders			
Fatigue [A] †	21/228 (9.21%)	13/231 (5.63%)	7/229 (3.06%)
Nervous system disorders			
Dizziness [A] †	11/228 (4.82%)	14/231 (6.06%)	0/229 (0%)
Headache [A] †	11/228 (4.82%)	10/231 (4.33%)	13/229 (5.68%)
Sedation [A] †	15/228 (6.58%)	11/231 (4.76%)	0/229 (0%)
Somnolence [B] †	22/228 (9.65%)	20/231 (8.66%)	0/229 (0%)
Tremor [A] †	0/228 (0%)	0/231 (0%)	15/229 (6.55%)

† Indicates events were collected by systematic assessment.
A Term from vocabulary, MedDRA (10.0)
B Term from vocabulary, MedDRA 10.0

Limitations and Caveats

[Not specified]

More Information

Certain Agreements:

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

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 less than or equal to 60 days from the time submitted to the sponsor for review. The sponsor cannot require changes to the communication and cannot extend the embargo.

Results Point of Contact:

Name/Official Title: Gerard Lynch
Organization: AstraZeneca
Phone:
Email: aztrial_results_posting@astrazeneca.com