Characteristics Table for The Clinical Question: In the treatment of GAD what pharmacological strategies are effective in preventing relapse (including maintenance treatment)?

Comparisons Included in this Clinical Question

Duloxetine (SNRI) vs. placebo
DAVIDSON2008

Duloxetine (SNRI) vs. Venlafaxine (SNRI)
DAVIDSON2008

Escitalopram vs Placebo
ALLGULANDER2006

Pregabalin vs Placebo
FELTNER2008

Quetiapine vs Placebo
ASTRAZENECA2008B

SSRI vs Placebo
STOCCHI2003

Venlafaxine (SNRI) vs. placebo
DAVIDSON2008

Characteristics of Included Studies

Methods	Participants	Outcomes	Interventions	Notes
ALLGULANDER2006 Study Type: RCT Study Description: 491 ppts received open-label escitalopram for 12 wk. 375 responded (HAMA score <=10) and were randomized to DB treatment with escitalopram or placebo. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 532 Setting: Multicentre (59 centres): multiple countries. Recruited by GPs, psychiatrists, and media advertisements. Outpatients. Notes: RANDOMISATION: randomised in a 1:1 fashion using computer generated randomisation list. Info on Screening Process: 424 completed open-label phase. 49 dropped out before DB phase: 8 due to AEs, 28 due to lack of efficacy, 3 withdrew consent, 5 did not comply and 5 for other reasons.	n= 375 Age: Mean 41 Range 18-65 Sex: 255 males 120 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV-TR Exclusions: Major depressive disorder, panic disorder, social anxiety disorder, PTSD, bipolar disorder, OCD, eating disorders, substance use disorder and any current or past psychotic disorder. Body dysmorphic disorder or any personality disorder. At risk of suicide or had made a suicide attempt within the past year. Unstable serious somatic illness and/or serious sequeale of liver or renal insufficiency were excluded. Pregnant or breastfeeding women. Notes: Treatment continued for 24-76 weeks until the patient relapsed or was withdrawn for other reasons. Relapse was defined as HAMA total score >=15. Was a 1 week screening period before open-label phase. Baseline: HAM-A at baseline. Escitalopram: 5.7 (3.9) and Placebo: 5.0 (3.1).	**Data Used** CGI-I HAMA Adverse events Sheehan Disability Scale (SDS) Hospital Anxiety and Depression Scale (anxiety) Leaving the study due to adverse events Leaving the study early for any reason Notes: Assessed at 1, 2 and 4 weeks and then every 4 weeks until last dose of DB treatment.	**Group 1 N= 187** Placebo - No details provided. **Group 2 N= 186** Escitalopram. Mean dose 20mg/day - 20mg/day.	Ppts who completed DB phase entered a 2 week taper period where escitalopram group received escitalopram 10mg/day for a week and placebo for 2nd week. Placebo ppts continued on placebo. Quality assessed: +. Funding: H. Lundbeck A/S.
ASTRAZENECA2008B Study Type: RCT Study Description: Efficacy of quetiapine SR in the maintenance treatment of patients with GAD Blindness: Double blind Duration (days): Mean 364 Setting: Asia, Europe, North America and Australia Notes: Randomization: no further details Info on Screening Process: 1811 screened, 433 randomized	n= 432 Age: Range 18-65 Sex: 151 males 281 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) Exclusions: HAM-A score >12, CGI-S score >3, MADRS score >16 Baseline: Not reported	**Data Used** SDS total score PSQI global score CGI-S Q-LES-Q 16 Q-LES-Q 15 Q-LES-Q maximum total score HAMA somatic anxiety cluster score HAMA psychic anxiety cluster score HAMA total score	**Group 1 N= 216** Quetiapine - Flexible dosing (50mg-300mg), periodic stepwise increases up to maximum of 300mg **Group 2 N= 216** Placebo	
DAVIDSON2008				

Study Type: RCT Study Description: Relapse prevention trial with a 26-week open ladel, felxible dose therapy followed by 26 week double-blind, placebo controlled contunuation therapy Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 182 Setting: Not reported Notes: RANDOMISATION: not reported ALLOCATION CONCEALMENT: interactive voice recognition system Info on Screening Process: Patients enrolled in open-label (N=887); 51.5% discontinued; 429 randomised in double-blind phase; 49/216 (23%) - duloxetine & 97/213 (46%) - placebo dropped out.	n= 429 Age: Sex: Diagnosis: Exclusions: - Patients who did not complete open label & met response criteria Exclusion criteria for open label trial: -<18 years - No primary DSM-IV diagnosis of GAD - CGI-S <4 - HADS anxiety subscale <10 - Covia Anxiety score <9 or not greater and then Raskin depression total score. Raskin depression scale item rated >3 - Medical illness that would contraindicate use of duloxetine - Women of childbearing age not using adequate contraception - recent diagnosis of depression or substance abuse/depence - past year history of panic disorder, PTSD or eating disorder - lifetime history of psychotic, bipolar, OCD or psychosis - lack of response of GAD to 2 prior adequate trails of antidepressants or benzodiazepine treatments - psychotherapy iniated 6 weeks prior to study enrollment Baseline: No differences at baseline.	**Data Used** Beck scale for suicide ideation HAMA Relapse Sheehan Disability Scale (SDS) Hospital Anxiety and Depression Scale (anxiety) Q-LES-Q-SF EQ-5D Leaving the study due to adverse events Notes: Relapse = (a) increase in CGI-S 2+ points to score 4+ while meeting criteria for GAD (MINI) or (b) discontinuation due to lack of efficacy. DROP OUTS: 49/216 (23%) - duloxetine; 97/213 (46%) - placebo	**Group 1 N= 213** Placebo - 2 week taper period. All patients received 4 capsules daily. **Group 2 N= 216** Duloxetine. Mean dose 60-120mg/day - Duloxetine continued at same doseas their open label phase treatment (between 60-120 mg/day). The paper does not report mean dose.	FUNDED BY ELI LILLY: Trial report collected (#7108). Quality assessed: +
Results from this paper:				
FELTNER2008 Study Type: RCT Study Description: 1 week screening phase followed by 8 weeks open label acute treatment phase, 24 week DB relapse prevention phase and 2 week discontinuation. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 245 Setting: Multicentre: USA (17 sites). Recrutied via advertisements in the local media. Notes: RANDOMISATION: no details provided. Info on Screening Process: 859 ppts screened: 624 enrolled in acute phase. 339 randomised to DB treatment. 285 discontinued before DB phase: 89 AEs, 19 lack of efficacy, 62 lost to follow-up, 48 withdrew consent, 32 didn't meet inc. criteria, 9 did not comply and 26 for other.	n= 339 Age: Mean 39 Sex: 145 males 193 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Current diagnosis of seizure disorder or a lifetime history of bipolar disorder, schizophrenia, psychotic disorder or factitious disorder. History within the past 6 months of any clinically significant Axis I disorder, including panic disorder and social anxiety disorder. Use of psychotropic medication within 2 weeks of visit 1. Patients at risk of suicide. Women who were pregnant or lactating. Currently undergoing psychotherapy. Notes: Ppts had GAD >1 year. Diagnosis based on MINI. Ppts scored >=20 on HAM-A, >=9 on Covi and <=7 on Raskin. Allowed ppts with dysthymia, depession NOS, or specific phobia. Baseline: HAM-A at baseline (for DB phase). Pregabalin: 5.9 (3.2) and Placebo: 5.5 (3.4).	**Data Used** CGI-I HAMA Adverse events Sheehan Disability Scale (SDS) Leaving the study due to adverse events Leaving the study early for any reason Notes: Assessed at 1 week screening phase and at weeks 1, 2, 4, 6, 7, 8, 9, 10, 11, 12, 14, 16, 20, 24, 28, 32, 33 and 34.	**Group 1 N= 168** Pregabalin. Mean dose 450mg/day - 150mg thrice daily. Received DB treatment for up to 6 months or until relapsed or discontinued treatment. **Group 2 N= 170** Placebo - Received pregabalin at 300mg/day for 3 days before complete placebo substitution. Received DB treatment for up to 6 months or until relapsed or discontinued treatment.	Funding: Pfizer, Inc. Quality assessed: +.
STOCCHI2003 Study Type: RCT Study Description: Single blind paroxetine for 8 weeks, followed by double blind RCT placebo or paroxetine for 24 weeks	n= 561 Age: Mean 43 Sex: 203 males 358 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV	**Data Used** HAMA Relapse Leaving the study due to adverse events Leaving the study early for any reason Remission (less than 7 on HAMA)	**Group 1 N= 287** Placebo - Single blind phase as paroxetine group. Double blind phase: underwent a 3-week taper and received placebo at week 4 of continuation phase.	Funding: GSK. Quality assessed: -.

Blindness: Double blind Duration (days): Mean 240 Setting: Outpatients from 47 centres including Finland, Norway, Denmark, Hungary, Greece, Italy, Czech Republic Notes: RANDOMISATION: no further details Info on Screening Process: 652 entered single blind phase, 566 entered double blind phase, 4 dropped out of the paroxetine group and 1 from placebo group	Exclusions: - HAM-A <20 - HAM-A items 1 and 2 <2 - MADRS > 17 - <20% improvement in HAM-A during single blind phase		**Group 2 N= 274** Paroxetine. Mean dose 28.1mg - Single blind phase: 20mg/day for 2 weeks then increase 10mg/day each week if needed up to 50mg/day. Double blind phase: continued treatment	

Characteristics of Excluded Studies

References of Included Studies

ALLGULANDER2006 (Published Data Only)

Allgulander, C., Florea, I., & Huusom, A.K.T. (2006) Prevention of relapse in generalized anxiety disorder by escitalopram treatment. International Journal of Neuropsychopharmacology, 9, 495-505.

ASTRAZENECA2008B (Published Data Only)

Astra Zeneca (2008) A multi-center, double-blind, randomized-withdrawal, parallel-group, placebo-controlled phase III study of the efficacy and safety of quetiapine fumarate sustained release (Seroquel SR) as monotherapy in the maintenance treatment of patients with generalized anxiety disorder following an open-label stabilization period (PLATINUM STUDY)

DAVIDSON2008 (Published Data Only)

Davidson, J.R.T., Wittchen, H.-U., Llorca, P.M. et al.(2008) Duloxetine treatment for relapse prevention in adults with generalized anxiety disorder: a double-blind placebo-controlled trial. European Neuropsychopharmacology, 18, 673-681

FELTNER2008 (Published Data Only)

Feltner, D., Wittchen, H-U., Kavoussi, R., Brock, J., Baldinetti, F., & Pande, A.C. (2008) Long-term efficacy of pregabalin in generalized anxiety disorder. International Clinical Psychopharmacology, 23, 18-28.

STOCCHI2003 (Published Data Only)

Stocchi, F., Nordera, G., Jokinen, R.H. et al. (2003) Efficacy and tolerability of paroxetine for the long term treatment of generalize anxiety disorder. Journal of Clinical Psychiatry, 64, 250-258.

References of Excluded Studies