

Antidépresseurs

Nouveaux médicaments de l'anxiété

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Trouble anxiété généralisé

Benzodiazépines

- Propriétés pharmacologiques
 - Agoniste des récepteurs $GABA_A$ couplés au canal chlore (hyperpolarisation neuronale)
 - o Effets anxiolytiques
 - o Effets sédatifs, hypnotiques
 - o Effets myorelaxants
 - o Effets anticonvulsivants

Benzodiazépines

- Effets secondaires
 - Sédation diurne
 - Ataxie, vertiges
 - Altération des performances cognitives
 - Réactions paradoxales (enfant, sujet âgé)
 - o Agitation
 - o Anxiété
 - o Irritabilité
 - o Agressivité

Benzodiazépines

- Intoxication
 - Somnolence
 - Difficultés d'élocution
 - Ataxie (démarche ébrieuse, incoordination motrice)
 - Dyspnée, dépression respiratoire
 - Confusion mentale, coma

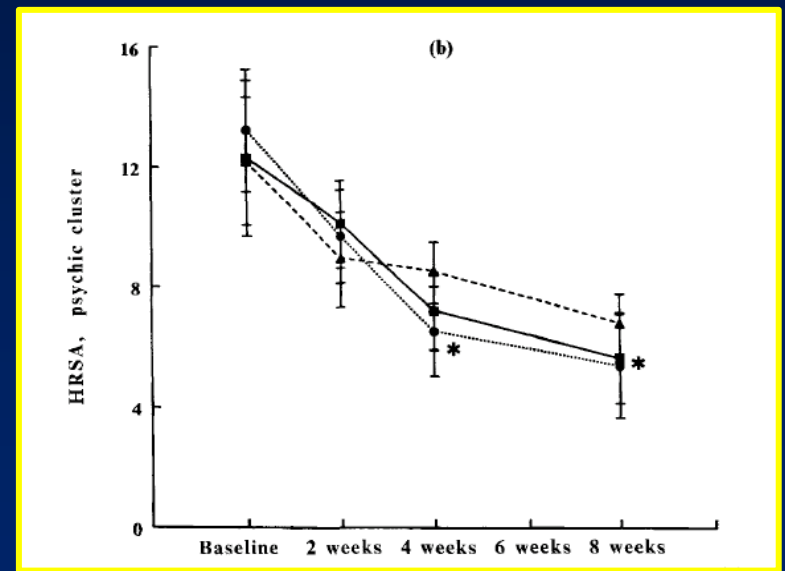
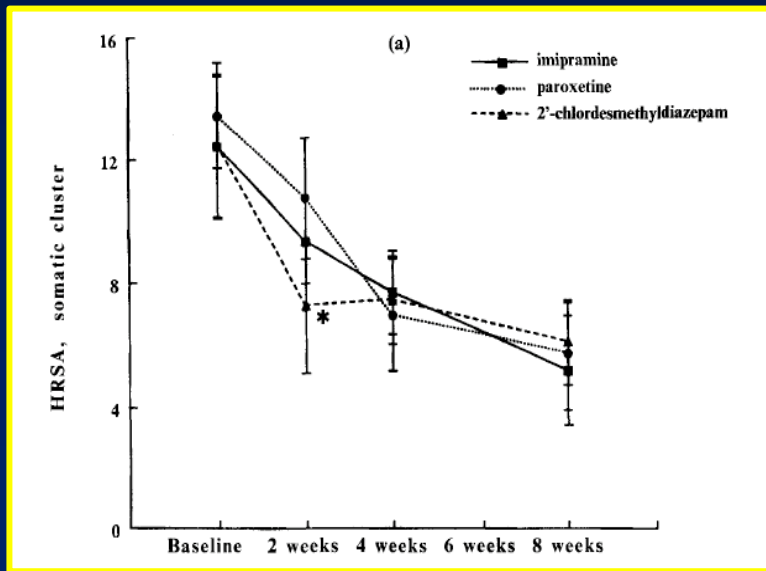
Benzodiazépines

- Sevrage
 - Anxiété, irritabilité, insomnie, fatigue
 - Céphalées
 - Douleurs musculaires
 - Tremblements, frissons
 - Sueurs
 - Vertiges
 - Difficultés de concentration
 - Nausées, perte d'appétit
 - Crises convulsives

Benzodiazépines

- Tolérance/dépendance
 - Effet notablement diminué en cas d'utilisation continue d'une même quantité de la même substance
 - o Rapidité des effets anxiolytiques après instauration du traitement (> placebo)
 - o Épuisement des effets anxiolytiques après 4-6 semaines de traitement (= placebo)

Benzodiazépines vs Antidépresseurs



Benzodiazépines vs Antidépresseurs

Side-effect	Paroxetine (%)	Imipramine (%)	2'-CD (%)
Constipation ^a	8	39	5
Dizziness	8	22	15
Drowsiness ^b	4	39	60
Dry mouth ^c	8	56	10
Nausea ^d	40	6	5
Nervousness	12	11	5
Tiredness	8	22	10
Other	8	11	10

2'-CD, 2'-chlordesmethyldiazepam.

^a $\chi^2 = 10.07$, $df = 2$, $P < 0.01$.

^b $\chi^2 = 13.61$, $df = 2$, $P < 0.01$.

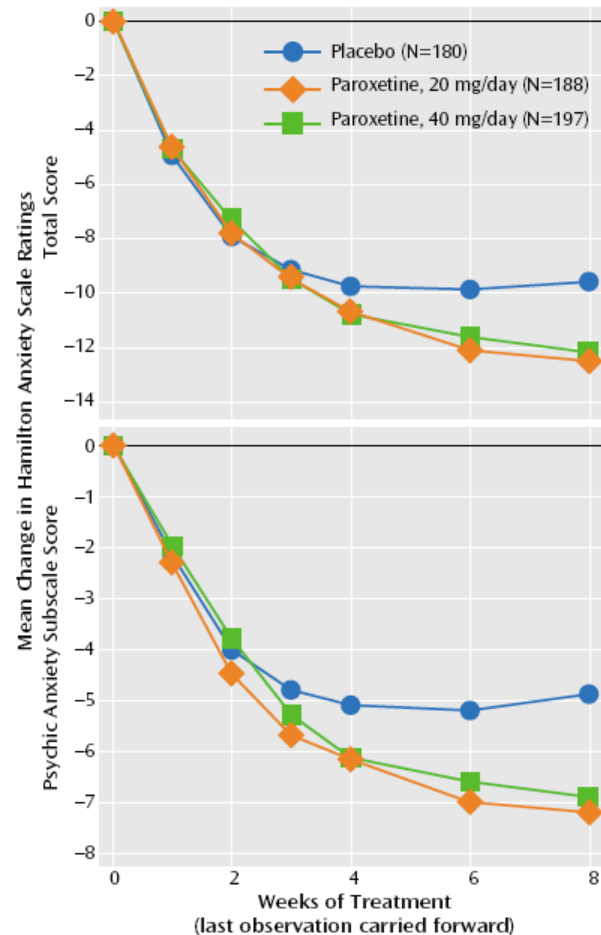
^c $\chi^2 = 16.23$, $df = 2$, $P < 0.001$.

^d $\chi^2 = 11.80$, $df = 2$, $P < 0.01$.

Paroxetine

(8 semaines)

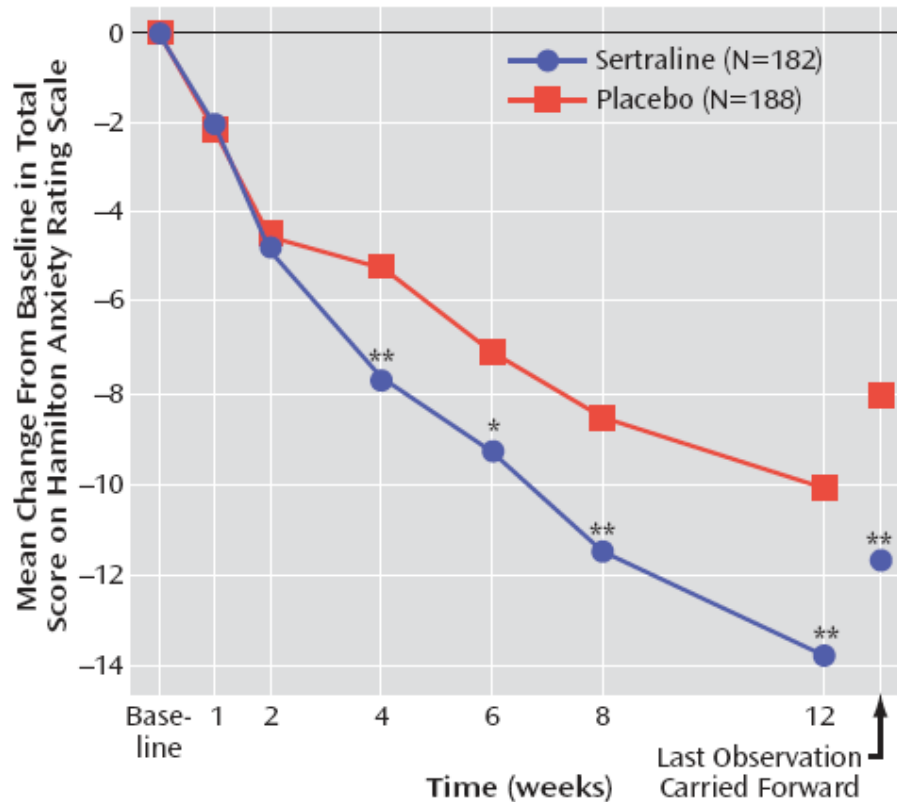
FIGURE 2. Symptom Improvement in Patients With Generalized Anxiety Disorder Randomly Assigned to 8 Weeks of Double-Blind Treatment With Paroxetine (20 or 40 mg/day) or Placebo



Sertraline

(12 semaines)

FIGURE 2. Change in Anxiety Score Across 12 Weeks of Treatment With Sertraline or Placebo for Patients With Generalized Anxiety Disorder^a



Sertraline
95,1 mg/j
(± 45,5)

Escitalopram (8 semaines)

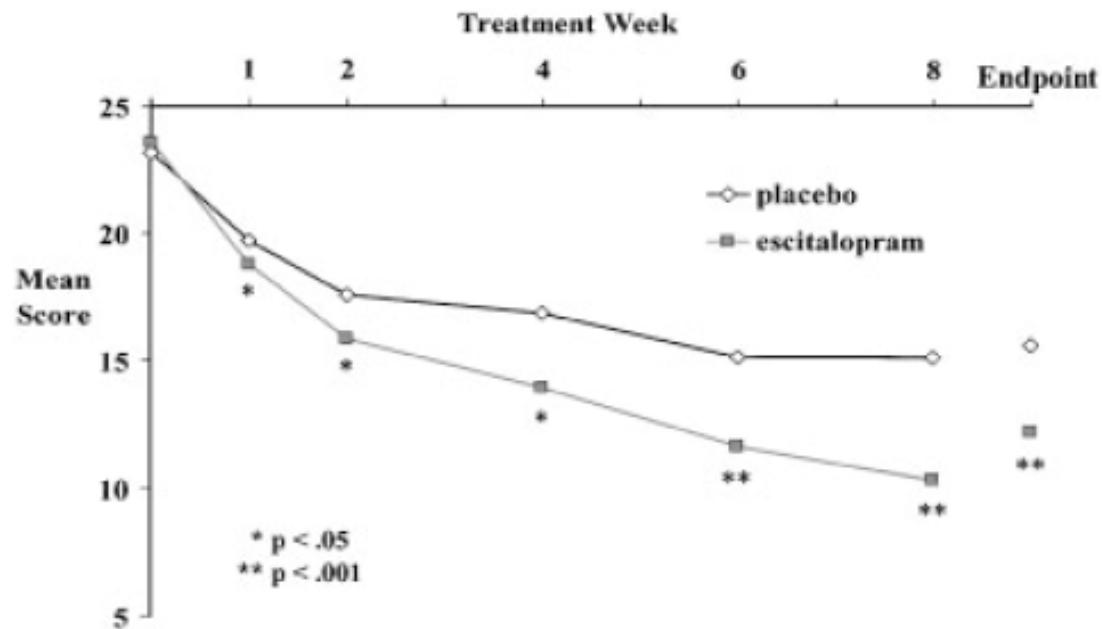
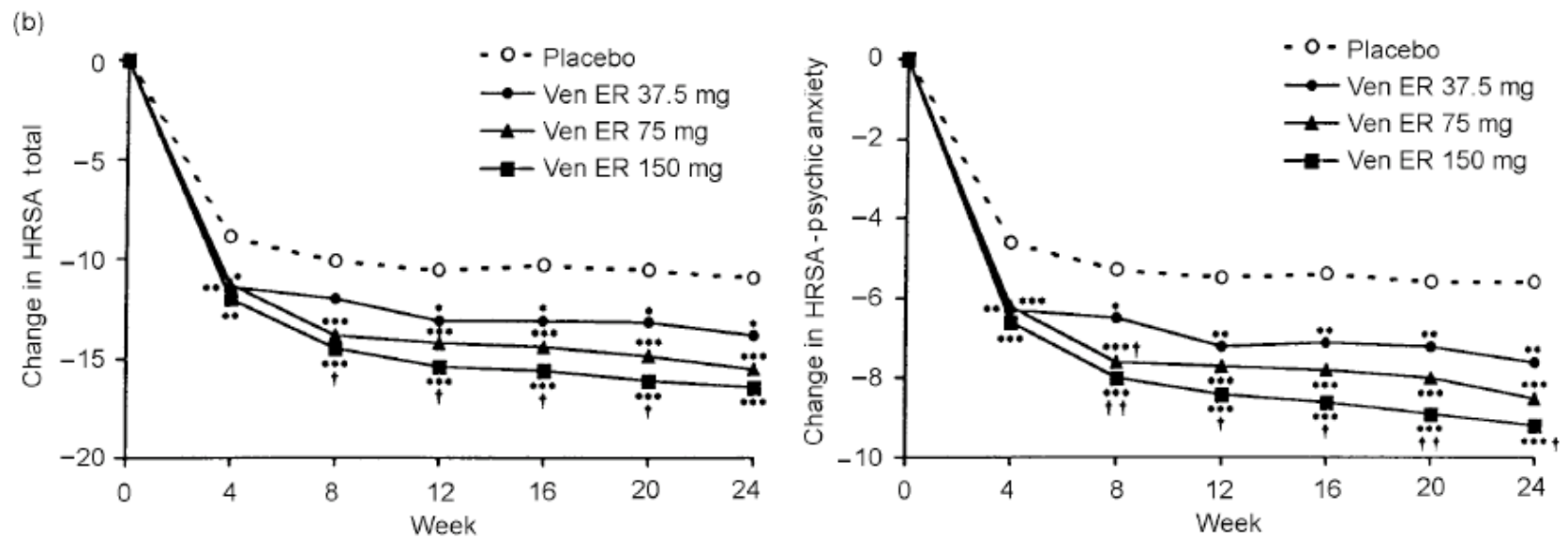


Figure 1. Mean HAMA scores by visit (Observed Cases) and at endpoint (week 8, LOCF) for patients treated with either placebo or escitalopram. * $P < .01$. ** $P < .001$.

Escitalopram
10-20 mg/j

Venlafaxine (24 semaines)



Recommendations

Table 7.5 Recommendations for pharmacotherapy for GAD

First-line	Paroxetine, escitalopram, sertraline, venlafaxine XR
Second-line	Alprazolam, bromazepam, lorazepam, diazepam, buspirone, imipramine, pregabalin, bupropion XL
Third-line	Mirtazapine, citalopram, trazodone, hydroxyzine Adjunctive olanzapine, risperidone
Not recommended	Beta blocker (propranolol)

Trouble panique

Recommendations

Table 3.7 Recommendations for pharmacotherapy for PD

First-line	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, venlafaxine XR
Second-line	Clomipramine, imipramine, mirtazapine, benzodiazepines (for example, alprazolam, clonazepam, lorazepam, diazepam), adjunctive clonazepam
Third-line	Divalproex, gabapentin, phenelzine, moclobemide, bupropion, adjunctive pindolol, olanzapine, risperidone, quetiapine
Not recommended	Buspirone, trazodone, propranolol, carbamazepine

Phobie sociale

Recommendations

Table 5.6 Recommendations for pharmacotherapy for generalized SAD

First-line	Escitalopram, fluvoxamine IR or CR, paroxetine IR or CR, sertraline, venlafaxine XR
Second-line	Clonazepam, alprazolam, bromazepam, gabapentin, pregabalin, citalopram, phenelzine
Third-line	Fluoxetine, bupropion, mirtazapine, moclobemide, divalproex, topiramate, levetiracetam, olanzapine, quetiapine, selegiline, clomipramine Adjunctive: risperidone, aripiprazole, tiagabine
Not recommended	Atenolol, propranolol, buspirone, imipramine, pergolide, St John's wort Adjunctive: pindolol, clonazepam

Trouble obsessionnel-compulsif

Recommendations

Table 6.6 Recommendations for pharmacotherapy for OCD

First-line	Fluvoxamine, fluoxetine, paroxetine, sertraline
Second-line	Clomipramine, venlafaxine XR, citalopram, mirtazapine, adjunctive risperidone
Third-line	IV clomipramine, escitalopram, phenelzine, tranylcypromine Adjunctive: mirtazapine, olanzapine, quetiapine, haloperidol, gabapentin, topiramate, tramadol, riluzole, St John's wort, pindolol
Not recommended	Clonazepam, desipramine, bupropion, clonidine, buspirone, lithium, naltrexone, adjunctive morphine

Trouble état de stress post-traumatique

Recommendations

Table 8.5 Recommendations for pharmacotherapy for PTSD

First-line	Fluoxetine, paroxetine, sertraline, venlafaxine XR
Second-line	Fluvoxamine, mirtazapine, moclobemide, phenelzine Adjunctive: risperidone, olanzapine
Third-line	Amitriptyline, imipramine, escitalopram Adjunctive: carbamazepine, gabapentin, lamotrigine, valproate, tiagabine, topiramate, quetiapine, clonidine, trazodone, buspirone, bupropion, prazosin, citalopram, fluphenazine, naltrexone
Not recommended	Desipramine, cyproheptadine Monotherapy: alprazolam, clonazepam, olanzapine

Conclusions

- Dans les troubles anxieux
 - Importance des antidépresseurs de la classe des inhibiteurs de la recapture de la sérotonine (\pm noradrénaline)
 - o Nouveaux médicaments de l'anxiété \ggg BZD

	BZD	ATD
Délai d'action	rapide	retardé
Tolérance	oui	non
Dépendance	oui	non
Effets secondaires (ex: cognitifs)	oui	non

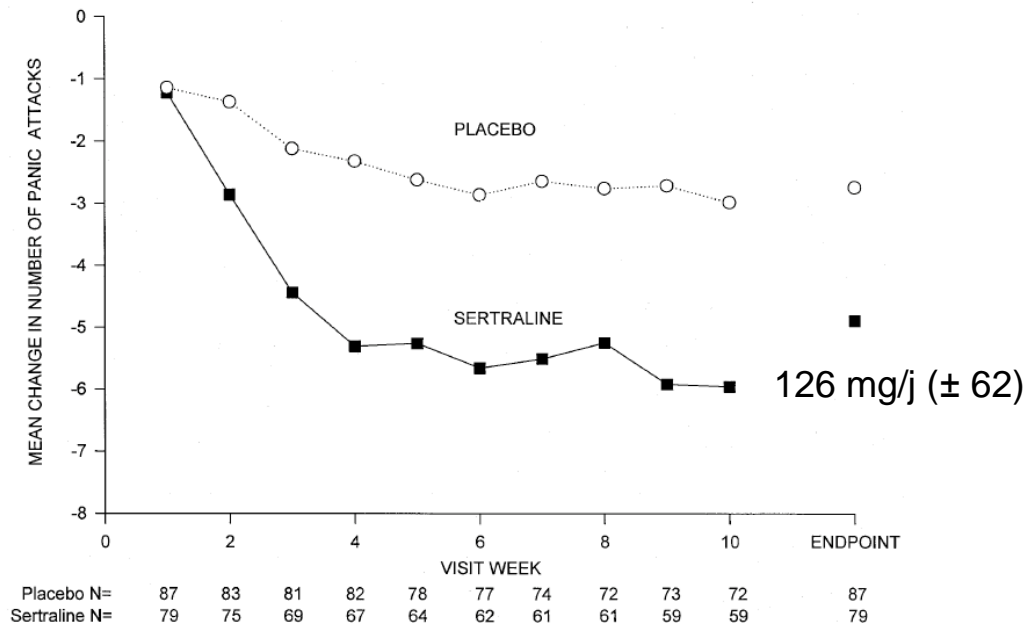
Quelques données de la littérature

Trouble panique

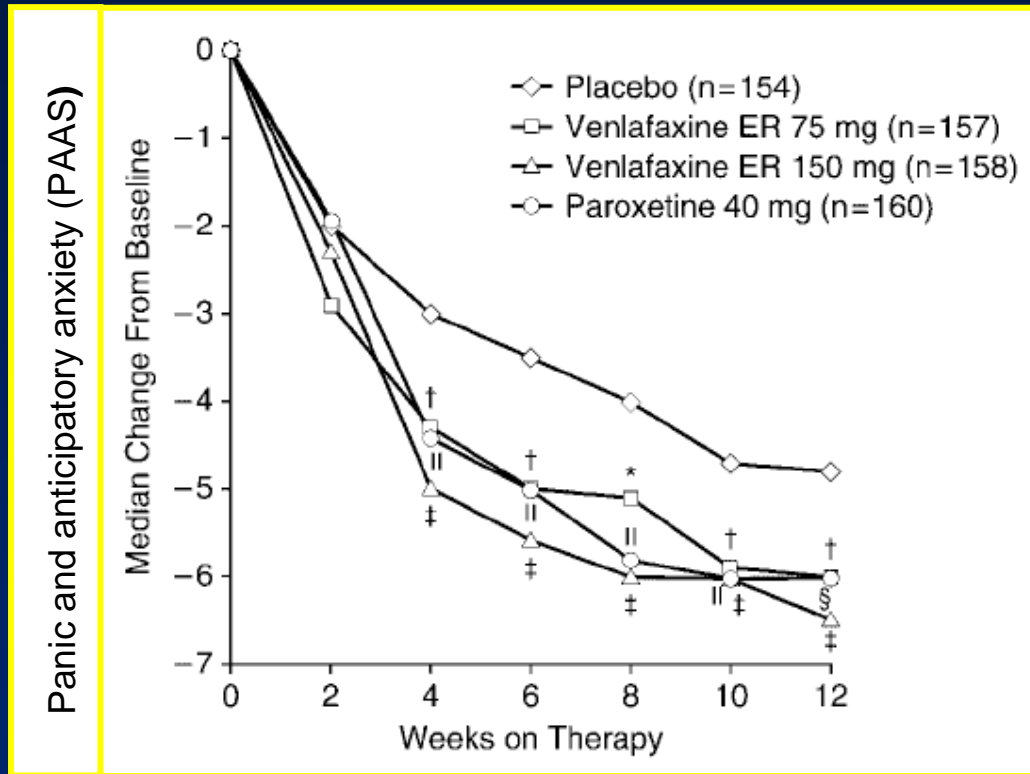
Sertraline

(12 semaines)

FIGURE 1. Mean Change From Baseline in Number of Panic Attacks per Week at Each Week and Endpoint (Observed Cases) for Patients With Panic Disorder Who Received Sertraline or Placebo^a



Venlafaxine/Paroxetine (12 semaines)

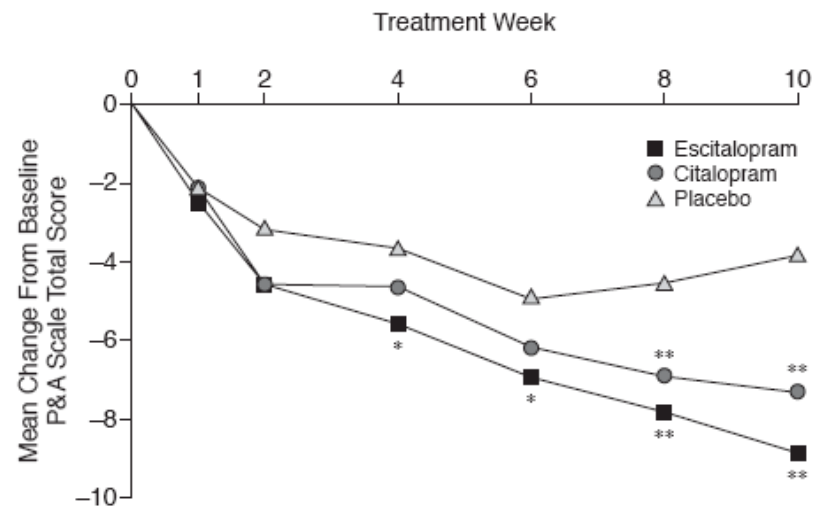


Escitalopram (10 semaines)

Escitalopram
10-20 mg/j

Citalopram
20-40 mg/j

Figure 1. Mean Changes From Baseline in Panic and Agoraphobia (P&A) Scale Total Score for Patients Treated With Escitalopram, Citalopram, or Placebo



* $p \leq .05$, escitalopram vs. placebo.

** $p < .01$, escitalopram or citalopram vs. placebo.

Venlafaxine

Rechute (26 semaines)

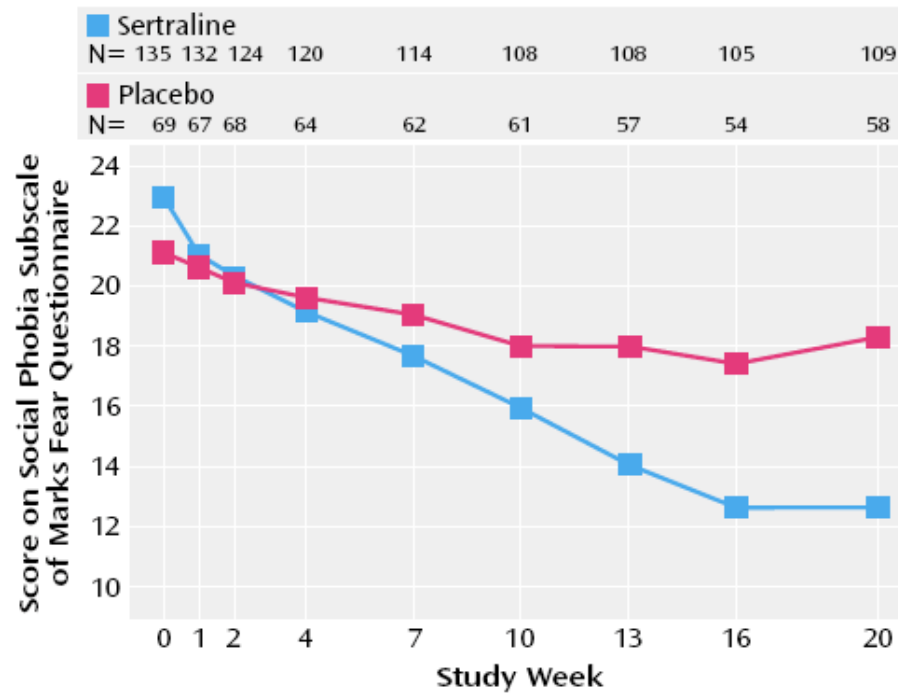
Traitement (26 semaines)	Rechute
Venlafaxine (n=89) (172,1 mg/j \pm 56,2)	20 (22,5%)
Placebo (n=80)	40 (50,0%)

Phobie sociale

Sertraline

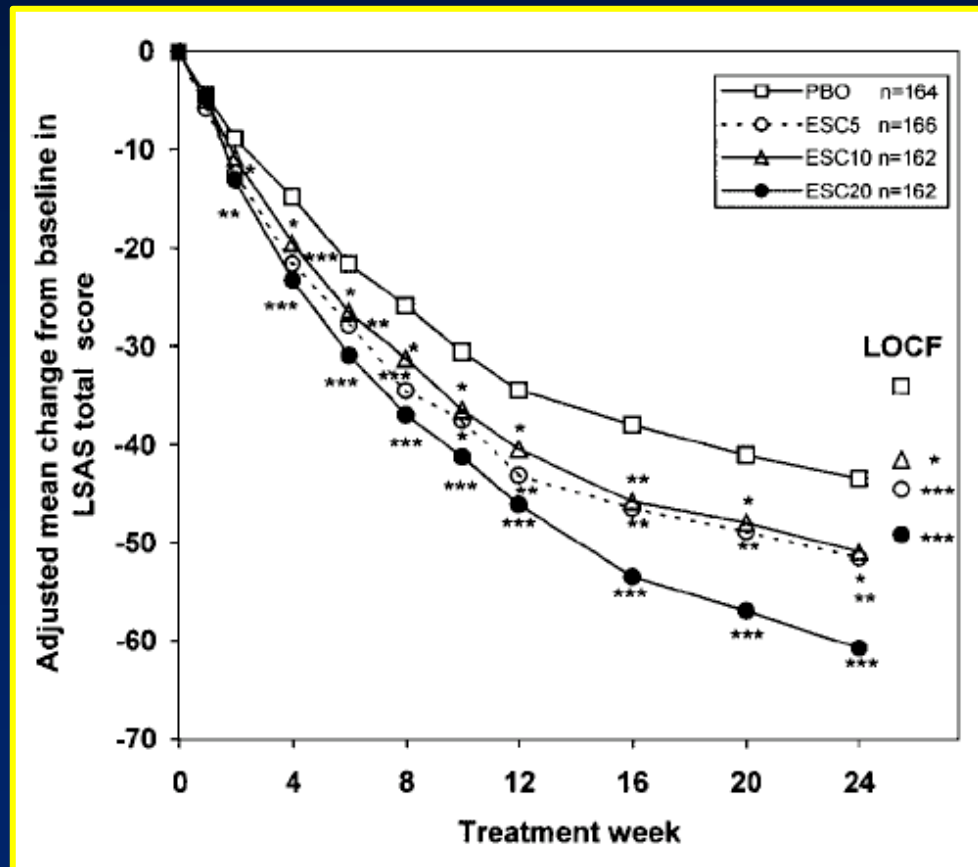
(20 semaines)

FIGURE 1. Ratings of Social Phobia in 204 Patients With Generalized Social Phobia Randomly Assigned to Receive Sertraline or Placebo Over a Period of 20 Weeks



Sertraline
146,7 mg/j
(± 57,0)

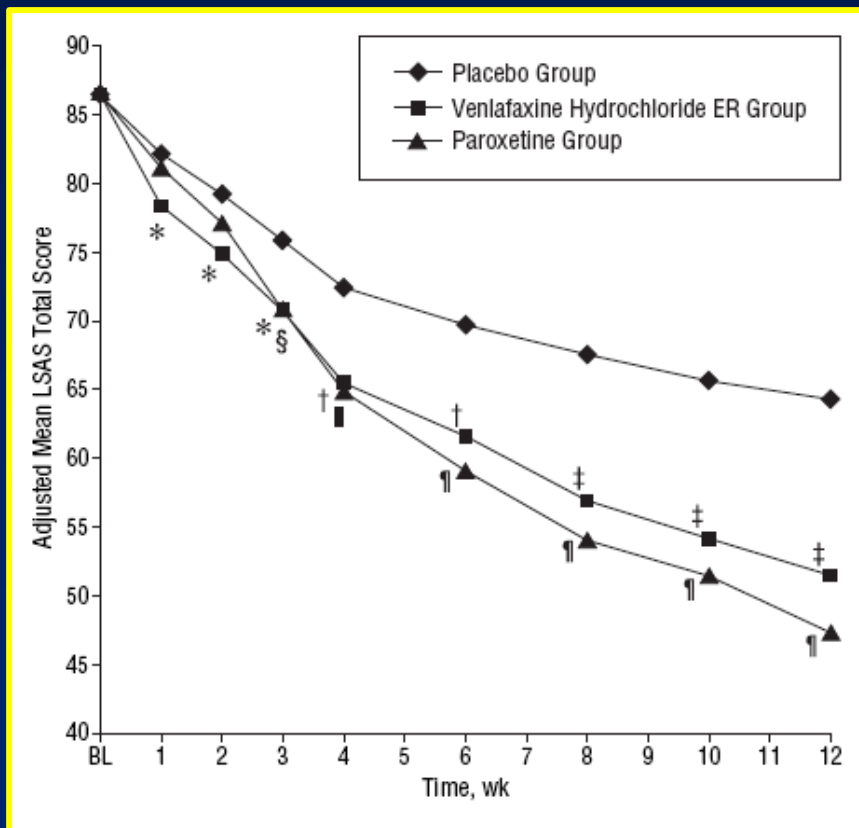
Escitalopram (24 semaines)



Venlafaxine/Paroxetine (12 semaines)

Venlafaxine
201,7 mg/j
($\pm 38,1$)

Paroxetine
46,0 mg/j
($\pm 7,9$)



Sertraline

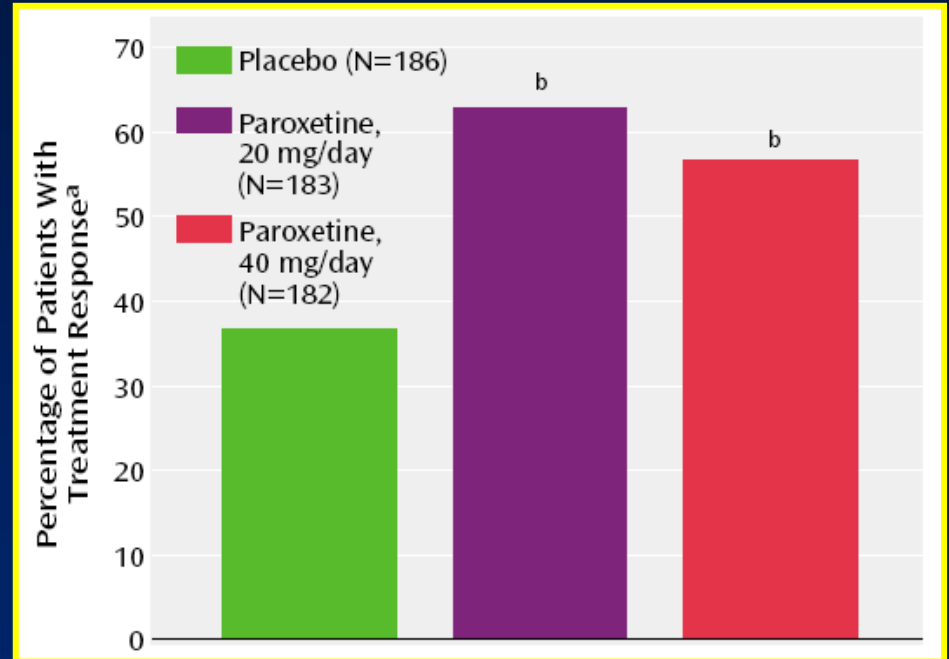
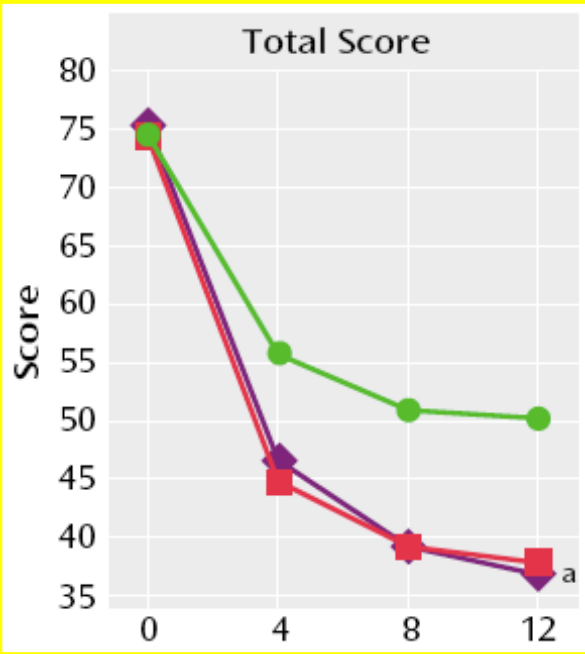
Rechute (24 semaines)

Traitement (24 semaines)	Rechute
Sertraline (n=25) (50-200 mg/j)	1 (4%)
Placebo (n=25)	9 (36%)

Trouble état de stress post-traumatique

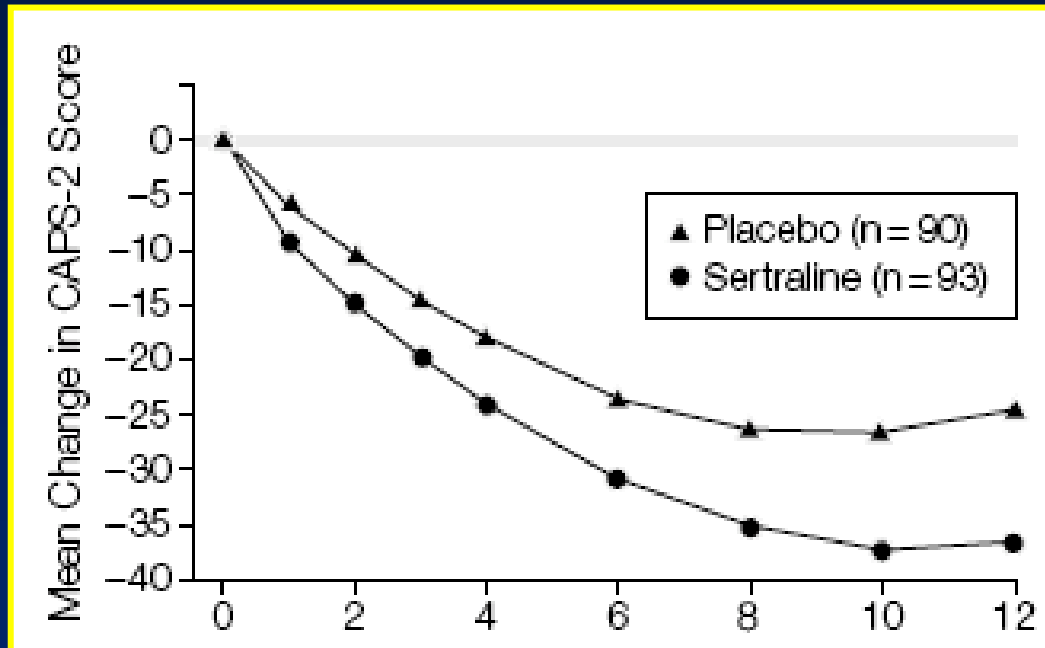
Paroxetine (12 semaines)

Clinician-administered PTSD scale
(CAPS)



Sertraline

(12 semaines)

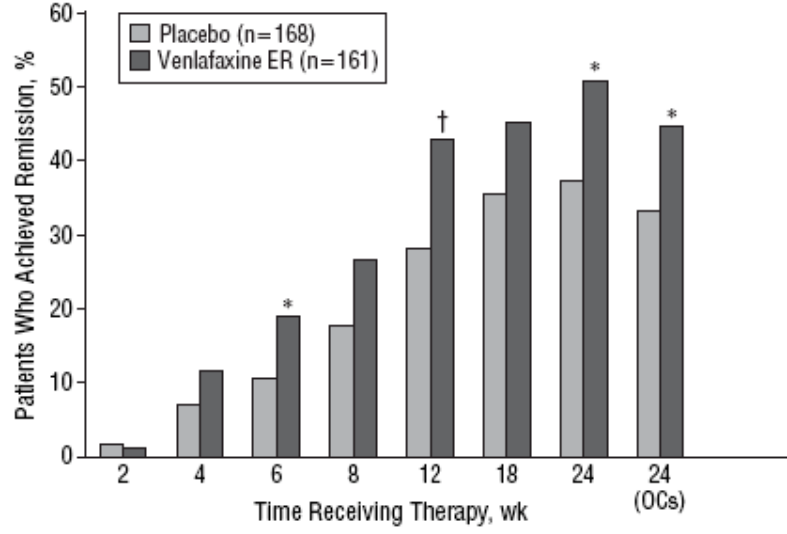
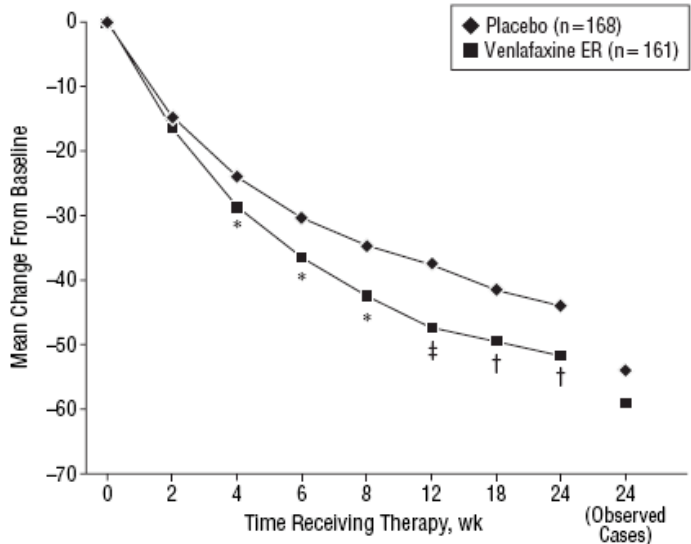


Sertraline
133,3 mg/j
($\pm 59,2$)

Venlafaxine

(24 semaines)

Venlafaxine
181,7 mg/j



Sertraline

Rechute (28 semaines)

Traitement (24 semaines)	Rechute
Sertraline (n=38) (137 mg/j \pm 52 mg/j)	2 (5,3%)
Placebo (n=46)	12 (26,1%)