Antidepressant efficacy may be enhanced with dual reuptake inhibition[1]

The new dual reuptake inhibitors (SNRIs), such as duloxetine, display a balance between serotonin (5-HT) and noradrenaline (NA) selectivity. These new antidepressants may offer improvements in efficacy, in the same way that the SSRIs introduced improvements in tolerability over the TCAs (through reduced affinity for alpha 1, histamine H 1 and cholinergic receptors). Figure 1

It is likely that dual reuptake inhibition is able to cover more of the symptoms experienced with depression. This greater spectrum of effectiveness may result in more responders and more remitters – resulting in an overall improvement in antidepressant efficacy.

Evidence from studies that combined the NA selective agent desipramine, with the 5-HT selective agent fluoxetine, demonstrated the improvements in efficacy that could be achieved with dual reuptake inhibition. Figure 2

This evidence for improved efficacy, and hence higher rates of remission, has already been demonstrated in clinical trials of duloxetine. Figure 3

Most depressed patients have a combination of both emotional and physical symptoms. Most of the scales used to assess depression in clinical studies have failed to bring the somatic aspect of depression to a level of attention equal to that of the psychological symptoms. Yet, 5-HT and NA play central roles in the neurophysiology of both emotional and physical symptoms prevalent in depression. Figure 4

Duloxetine, with its balanced 5-HT and NA reuptake inhibition, has demonstrated efficacy in relieving both the emotional and the physical symptoms of depression.

There is growing evidence that two neurotransmitters are probably better than one for treating depression.

The greater efficacy seen with dual reuptake inhibitors, such as duloxetine, may be associated with improved effects on a wider range of symptoms (including painful physical symptoms) and with better protection against relapse.

References

1. *Nutt, D. Dual acting antidepressants : efficacy and mechanisms. Presentation by David Nutt, Professor of Psychopharmacology, University of Bristol, 2005*

Figure 1

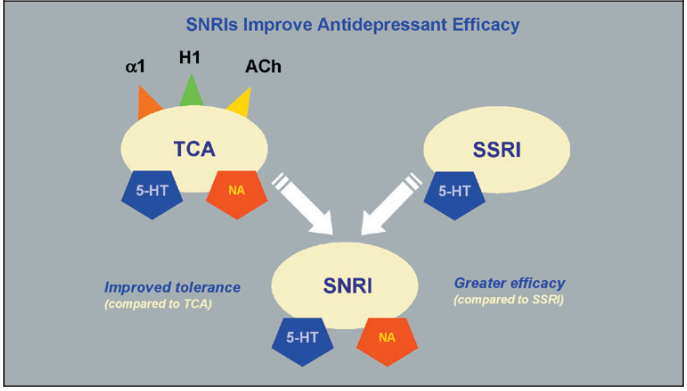

Figure 2

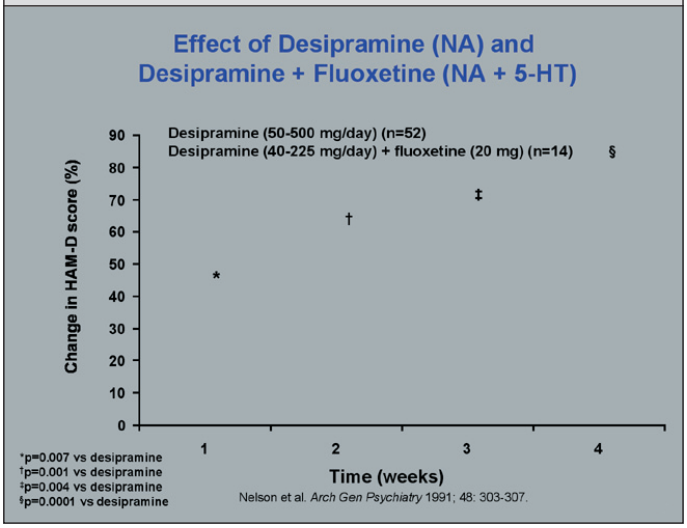

Figure 3

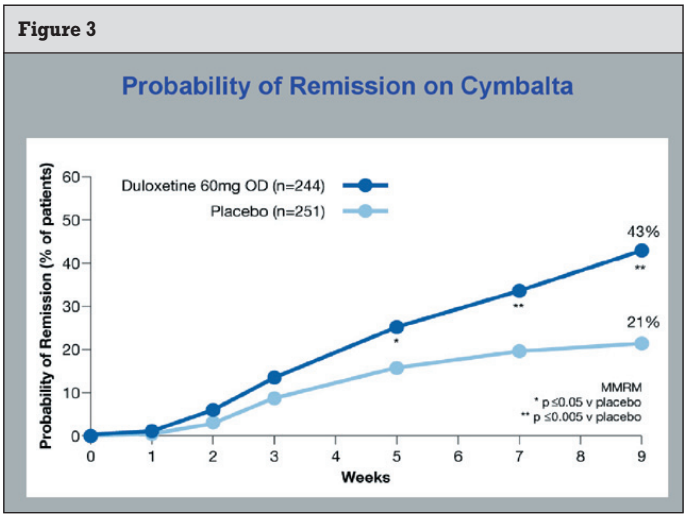

Figure 4

Depression Symptom Domains and Neurotransmitter Systems

	Physical	Psychological	Behavioural
NA	Fatigue Sleep disturbance Psychomotor agitation / retardation	Reduced concentration Reduced attention	Reduced productivity
5-HT + NA	Pain Appetite / weight change	Depressed mood Anxiety / nervousness Lack of pleasure / interest	Reduced leisure activities Social withdrawal Avoidant / fearful behaviour
5-HT	Headaches Muscle tension	Hopelessness Suicidal thoughts Anger attacks Irritability	Suicidal acts Violent / assaultive behaviour Compulsive behaviours Self-injury / mutilation