Commentary

Monotherapy with a selective serotonin reuptake inhibitor (SSRI) is the first line treatment for acute episodes of depression, and has a response rate in the region of 65%.[1] For depressed patients with an inadequate response, who do not respond at all, or who cannot tolerate treatment with an SSRI, switching to a dual mechanism of action antidepressant, such as venlafaxine, is a common second line strategy. The study by Thase *et al* demonstrates the advantages of a considered approach when switching to venlafaxine. The benefits of an improved initial response with a higher dose need to be balanced against the dose-related tolerability profile. The benefits of the higher dose strategy were modest and not well sustained after the first eight weeks of treatment, suggesting that the standard dose strategy may be more suitable than the high dose strategy for most patients. Increasing the dose is a suggested second line strategy for patients who have not responded to a standard dose of monotherapy. There may be stronger evidence to support a positive association between dose and response for venlafaxine than for other antidepressants.[2] However this study suggests that there is limited benefit when switching to venlafaxine in using escalating doses. Yet individual patients may benefit significantly from switching to high dose venlafaxine and this option should be considered on a case-by-case basis.

The finding of a significant difference using a global measure, the Clinical Global Impressions scale (CGI), but not the Hamilton Depression Rating Scale (HAM-D) is interesting. It is not the first time that such a pattern has been seen in a trial, and suggests both the value of the CGI as a metric, and that improvements may be in a domain outside of those measured by primary measures such as the HAM-D.

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1 Dodd S, Berk M. Predictors of antidepressant response: a selective review. *Int J Psych Clin Pract* 2004;**8**:91–100.
2 Berney P. Dose-response relationship of recent antidepressants in the short-term treatment of depression. *Dialogues Clin Neurosci* 2005;**7**:249–62.