Rapid response to Methylphenidate as an add-on therapy to mirtazapine in the treatment of major depressive disorder in terminally ill cancer patients: A four-week, randomized, double-blinded, placebo controlled study.

Reference: Ng Chong Guan, Marco PM Boks, Kit CB Roes, Nor Zuraida Zainal, Ahmad Hatim Sulaiman, Tan Seng Beng, Niek J de Wit. European Neuropsychopharmacology 2014; 24: 491-8.

Abstract
Background: This is a 4 week, randomized, double-blind, placebo-controlled study to examine the effects of methylphenidate as add-on therapy to mirtazapine compared to placebo for treatment of depression in terminally ill cancer patients.

Methods: It involved 88 terminally ill cancer patients from University of Malaya Medical Centre, Kuala Lumpur, Malaysia. (MADRS) score from baseline to day 3 was analyzed by linear regression. Changes of MADRS and Clinical Global Impression-Severity Scale (CGI-S) over 28 days were analyzed using mixed model repeated measures (MMRM). Secondary analysis of MADRS response rates, defined as 50% or more reduction from baseline score.

Results: A significantly larger reduction (MADRS) score in the methylphenidate group was observed from day 3 (B=4.14; 95% CI=1.83–6.45). Response rate (defined as 50% or more reduction from baseline MADRS score) in the methylphenidate treated group was superior from day 14. Improvement in Clinical Global Impression-Severity Scale (CGI-S) was greater in the methylphenidate treated group from day 3 until day 28. The drop-out rates were 52.3% in the methylphenidate group and 59.1% in the placebo group (relative risk=0.86, 95% CI=0.54–1.37) due to cancer progression. Nervous system adverse events were more common in methylphenidate treated subjects (20.5% vs 9.1%, p=0.13).

Conclusion: In conclusions, methylphenidate as add on therapy to mirtazapine demonstrated an earlier antidepressant response in terminally ill cancer patients, although at an increased risk of the nervous system side effects.

Strengths:
- Randomized, double-blinded, placebo controlled
- Multiple outcome measurements with same assessment tool over 28d period
- Baseline characteristics same in both groups

Weaknesses:
- High drop out rates for both groups (due to cancer progression, adverse events, withdrawn)
- Clinically relevant considered limited lifespan
- Diagnosis of depression confounded by cancer fatigue, lack of concentration, weight loss, decreased appetite
- Social supports not explored
- Needed 120 pts to power the study

Relevance to palliative care: Terminally ill patients experience a lot of distress and psychological suffering due to physical symptoms and poor prognosis. Conventional antidepressants are hampered by slow response rate. Need to consider risk/benefit for each patient on an individual basis, considering social supports and adverse events.