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Response to Grech et al.: FLOUX -PMS study sample considerations

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Dear Editor,

We thank Grech and colleagues¹ for questioning whether exclusion of multiple sclerosis (MS) patients with depression may be responsible for the unexpected low progression rate in the placebo group in the fluoxetine in progressive multiple sclerosis (FLUOX-PMS) study.² They refer to the biological similarities of inflammation in depression and relapsing MS.

However, very little research has been done on the relationship between depression and accumulation of disability in patients with progressive MS, which appears to occur independently of inflammation. A small retrospective study including both relapsing and progressive MS patients found no relationship between depression and disease progression over a period of 10 years.³ More research on the relationship between depression and the progressive disease component of MS would be needed to answer the question raised by Grech and colleagues. In addition, even with this knowledge, including untreated depressed MS patients in a 2-year placebo-controlled trial with antidepressant drug would be difficult to accept from an ethical point of view. In accordance with Chataway et al., we also think that, based on current knowledge, future sample size calculations in progressive MS studies using the combined timed 25-foot walk (T25FW) and 9-hole peg test (9HPT) endpoint should rather start from a 35%–40% progression rate instead of a 55% progression rate in the placebo group for a 2-year study.⁴

We agree with Grech and colleagues that the similarities between inflammatory aspects of relapsing MS

and depression are intriguing. In a double-blind, placebo-controlled exploratory study in patients with relapsing MS, we found that fluoxetine tended to reduce the formation of new enhancing lesions on brain magnetic resonance imaging (MRI).⁵ In the Multiple Sclerosis-Secondary Progressive Multi-Arm Randomization Trial (MS-SMART), a decreased number of new/enlarging T2 lesions was found at 96 weeks in patients treated with fluoxetine compared to placebo (reported on the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) 2018 by Chataway). A meta-analysis suggested that selective serotonin reuptake inhibitors (SSRIs) may reduce the relapse rate in patients with MS.⁶ Therefore, further research on disease-modifying aspects of fluoxetine may still be worthwhile but should, in first instance, focus on the inflammatory component of the disease.

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References

1. Grech LB, Butler E, Stuckey S, et al. Letter to the editor: FLOUX-PMS study sample considerations. *Mult Scler* 2019; 25: 1819–1820.
2. Cambron M, Mostert J, D'Hooghe M, et al. Fluoxetine in progressive multiple sclerosis: The FLUOX-PMS trial. *Mult Scler* 2019; 25: 1728–1735.

3. Koch M, Uyttenboogaart M, van Harten A, et al. Fatigue, depression and progression in multiple sclerosis. *Mult Scler* 2008; 14: 815–822.
4. Chataway J, Weir CJ and Fox RJ. The FLUOX-PMS trial: Underestimating the challenge in progressive multiple sclerosis trials. *Mult Scler* 2019; 25: 1697–1699.
5. Mostert JP, Admiraal-Behloul F, Hoogduin JM, et al. Effects of fluoxetine on disease activity in relapsing multiple sclerosis: A double-blind, placebo-controlled, exploratory study. *J Neurol Neurosurg Psychiatry* 2008; 79(9): 1027–1031.
6. Foley P, Lawler A, Chandran S, et al. Potential disease-modifying effects of selective serotonin reuptake inhibitors in multiple sclerosis: Systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry* 2014; 85(6): 709–710.

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Response to de Groot ‘There is an urgent need for palliative care specialists in MS – Commentary’

Date received: 20 August 2019; accepted: 26 August 2019

Dear Editor,

The recent articles published in the Controversies in Multiple Sclerosis section highlights the common concerns of when and how palliative care should be provided to patients with multiple sclerosis (PwMS).^{1–3} We are in support of the position taken by Solari and Pucci in supporting the need for palliative care specialists in MS.

In Malaysia, like in many other countries, palliative care is commonly accessed through a referral-based pathway instead of the integrated approach described by Solari and Pucci.^{2,4} We have observed that in practice, the existing referral-based palliative care pathway more commonly hinders, rather than facilitating access to palliative care.⁵

We identified that for the successful delivery of palliative care to happen, (1) a PwMS must present with a palliative care need, (2) the neurologist must perceive that need and make a referral and (3) the palliative care physician (PCP) must be willing to manage that need. Gaining access to palliative care through this ‘referral gauntlet’ requires that (a) the role of palliative care in MS is recognised and (b) there is a

consensus by PwMS, neurologists, and PCPs of the perceived needs. Predictably, this rarely happens. We illustrate three, suboptimal scenarios that commonly occur instead (see Figure 1).

Scenario 1: A patient is suffering from the symptoms of MS. While the patient and the neurologist recognise the need for symptomatic relief, neither of them see the role of palliative care in managing it. Consequently, palliative care is not asked for, not referred to and not provided.

Scenario 2: A patient experiences needs that are not perceived by the neurologist (for a variety of reasons). These needs are neither addressed nor is the patient referred to palliative care. Both the patient and the PCP remain out of each other’s reach as the lack of a neurologist referral creates a gap that is too wide to bridge.

Scenario 3: A severely ill PwMS requires help with advance care planning and end-of-life care, but being unable to travel, they cannot see a neurologist for an assessment and referral to palliative care. Consequently, palliative care is not received, despite the willingness to refer and to provide it.

These scenarios highlight the irrationality of using a referral-based care pathway for providing palliative care to PwMS. Unless palliative care is delivered through an integrated model of care where PCPs and neurologists provide care to PwMS together, palliative care will remain out of reach, no matter what the global guidelines and consensus statements say.

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