



## Primary Progressive Multiple Sclerosis (Topics in Neuroscience)

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"Why are there no effective treatments for my condition? Why do researchers exclude patients with primary progressive multiple sclerosis from enrolling in clinical trials? Please let me know if you hear of studies that I might be allowed to enter or treatments that I could try for my condition. " Thus, in recent years, the sad lament of the patient with primary progressive MS (PPMS). This variant, often in the guise of a chronic progressive myelopathy or, less commonly, progressive cerebellar or bulbar dysfunction, usually responds poorly to corticosteroids and rarely seems to benefit to a significant degree from intensive immunosuppressive treatments. In recent years, most randomized clinical trials have excluded PPMS patients on two counts. Clinical worsening develops slowly in PPMS and may not be recognized during the course of a 2-or 3-year trial even in untreated control patients. This factor alone adds to the potential for a type 2 error or, at the very least, inflates the sample size and duration of the trial. In addition, there is mounting evidence that progressive axonal degeneration and neuronal loss (rather than active, recurrent inflammation) may be important components of the pathology in this form of the disease. Although contemporary trials are evaluating whether PPMS patients may benefit from treatment with the  $\alpha$ -interferons and glatiramer acetate, preliminary, uncontrolled clinical experience suggests that the results may not be dramatic.

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