

High-Dose Cyclophosphamide in the Treatment of Aggressive Multiple Sclerosis: P01.072

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OBJECTIVE: We have explored the safety of high-dose cyclophosphamide without transplantation in patients with aggressive MS **BACKGROUND:** Multiple sclerosis (MS) is an autoimmune disease characterized by progressive immune-mediated destruction of myelin and axons within the CNS. Most patients on conventional immunomodulatory therapy continue to accrue progressive disability. Although immunoablation strategies transplantation may be effective in some patients in halting disease and inducing stable remission, these strategies are associated with unacceptable mortality rates, precluding the use of this treatment in most patients. Additionally, long-term conventional immunomodulatory treatment and immune ablation with transplantation are exceedingly expensive therapies and may result in only temporary disease suppression.

DESIGN/METHODS: Open-label trial of patients with aggressive MS given an up-front regimen of 50 mg/kg/d for four consecutive days. Enrolled patients must have aggressive MS as defined by 2 or more total gadolinium enhancing lesions on each of two pretreatment MRI scans; at least one clinical exacerbation in the last year despite being on conventional MS therapy; and sustained increase of ≥ 1.0 on the EDSS in the preceding year. **RESULTS:** Eight patients have completed the cyclophosphamide administration and none has had an unexpected grade 3 or 4 adverse event. All patients developed transient severe neutropenia, an expected consequence, followed by immune reconstitution in 10–17 days. All patients have had a reduction or elimination of new and enhancing lesions on the MRI. Brain atrophy has been slowed in several patients. No patient has had a clinical exacerbation following treatment and most patients have had a reduction in EDSS and an improvement in the MSFC following treatment. We are currently analyzing changes in microglial activation after HiCy using [^{11}C]-R-PK11195-PET imaging.

CONCLUSIONS/RELEVANCE: We conclude that this upfront regimen of cyclophosphamide in aggressive MS is worthy of further study as an alternative to immunoablative strategies with SCT.

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