Reply to Sormani et al

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We thank Drs Sormani, Bruzzi and Mancardi for their critical comments. They claim that large part of the neurotoxic effects described in our study may be due to:

a) detrimental effects of radiation,
b) a bias introduced by the observational nature of our study and possible unequilibrium of baseline features of the matched samples we compared in our study.

Ad a) : We agree that radiation may have added to the toxicity of chemotherapy and have discussed that transparently providing the appropriate references (3,4, 24-29, 46 and 48 in [1]) and not "shyly" as insinuated in the letter… As they may have noted, we and others also included patients who underwent chemotherapy without irradiation [6]. Again we observed a clear cut increase of blood neurofilament levels as a marker of neuronal damage [1].

Ad b) : clearly, an unequilibrium - especially of unknown confounding factors - is always a concern if the setting of non randomized observational studies [7, 8]. However, the slight and non significant difference in brain volumes Sormani *et al* pointed out is well in the range of variability observed even in the setting of randomized patient groups in MS [8]. Interestingly, the other outcome of our study neurofilament levels was also in some imbalance, but in the opposite direction: in the SPMS-PL group, baseline values were 65% higher than those in the SPMS-BMT patients [1]. More importantly, both the neurofilament increase and brain volume reduction we observed in the year after BMT were so clearly different and accompanied by clinical deterioration (EDSS dropped abruptly after conditioning and this drop was sustained over years [1,7]) that there is no reason to doubt about the fact of the occurrence of a related neurotoxicity.

References

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