**Supplemental data**

**Supplemental table 1: Basic CSF parameters**

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|  | Natalizumab cohort  before NTZ  (n= 26) | Natalizumab cohort  during NTZ  (n=49) | untreated  (n=47) |
| Median cell count (cells/µl) | 6  (range 0-60) | 2  (range 0-7) | 5  (range 0-136) |
| Median total protein (mg/dl) | 38  (range 23-78) | 38  (range 21-71) | 45  (range 23-105) |
| Blood-brain barrier dysfunction  Mild: albumin ratio < 10×10-3  Moderate: albumin ratio < 20×10-3  severe: albumin ratio > 20×10-3 | None: n=22 (81%)  Mild: n=4 (15%)  Moderate: n=1 (4%) | None: n=44 (90%)  Mild: n=4 (8%)  Moderate: n=1 (2%) | None: n=35 (75%)  Mild: n=11 (23%)  Moderate: n=1 (2%) |

**Supplemental Figure 1:** **Natalizumab treatment reduces serum IgM levels.** **(A)** Longitudinal analysis of patients before and during NTZ treatment (for IgG: n=28, mean therapy duration 4.7 years, for IgM: n=13, mean therapy duration 3.7 years, for IgA: n=12, mean therapy duration 3.8 years). Serum IgG and IgM decreased significantly during NZT treatment, albeit with a much stronger effect for IgM (p=0.0159, p=0.0005, respectively). IgA levels remained stable. Wilcoxon matched-pairs signed rank test. **(B)** Serum Ig of untreated and NTZ treated MS patients. IgG: 47 untreated, 49 NTZ treated patients (mean therapy duration 5.1 years), IgM: 41 untreated, 47 NTZ treated patients (mean therapy duration 5.0 years), IgA: 41 untreated, 47 NTZ treated patients (mean therapy duration 5.0 years). Serum IgM levels were considerably lower in the NTZ treated cohort (p<0.0001) while IgG- and IgA values were comparable. Mann-Whitney U test. Overall number of patients with Ig levels below reference values during NTZ treatment: IgG 4 patients, IgM 13 patients and IgA one patient. Dotted horizontal lines in **A** and **B** represent upper and lower reference values.