BRAIN VOLUME CHANGE AND DISABILITY IN FINGOLIMOD TRIALS

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10.1136/jnnp-2014-309236.138

Objective Investigate relationships between Brain Volume (BV) loss and clinical and MRI outcomes observed in three phase 3 fingolimod trials.

Method Percentage BV change (PBVC) was measured in the core-phases and extensions of FREEDOMS, FREEDOMS II and TRANSFORMS using 'Structural Image Evaluation Normalization, of Atrophy'. During the core-phases, correlations were assessed between PBVC and: cumulative Gd+-lesion count (LC); T2-lesion volume change (LVC); new/enlarging T2-LC; T1-hypointense LVC; number of confirmed relapses; EDSS score change; and MSFC score change.

Proportions of patients with 3- or 6-month confirmed disability progression (CDP) and correlations between PBVC and EDSS were determined.

Results In FREEDOMS, FREEDOMS II and TRANSFORMS, PBVC consistently correlated best with cumulative Gd+-LC ($p < 0.0001$), new/enlarging T2-LC ($p < 0.0001$) and number of confirmed relapses ($p < 0.005$). PBVC correlated with EDSS and MSFC in FREEDOMS ($p < 0.001$), and with MSFC in FREEDOMS II ($p = 0.016$). In combined study data PBVC correlation with EDSS strengthened over time (month 48, $p = 0.0001$). Stronger correlation was seen in patients with 3- or 6-month CDP (month 48, $p < 0.0001$).

Conclusion BV loss was greatest in patients who relapsed or who developed new Gd+ or T2-lesions. By reducing BV loss, fingolimod may slow disability progression.