

Efficacy of Ofatumumab on Microglial Activity in Patients with Relapsing forms of Multiple Sclerosis: Interim Analysis

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OBJECTIVE

Determine the effect of ofatumumab on microglial activation using [F-18]PBR06 PET targeting 18kilodalton-translocator protein (TSPO) in RMS patients.

BACKGROUND

The potential impact of ofatumumab on microglial activation in MS is unknown.

DESIGN/METHODS

20 [F-18]PBR06 PET scans in 5 RMS patients (mean age 40.2±12 years, 4 females, median EDSS 3.0, mean T25FW 4.25±0.54 seconds) were performed prior to, and at days 5, 28 and 90 after initiating ofatumumab. Peripheral CD19 counts and clinical evaluations were also performed. Individualized z-score maps of brain parenchymal microglial activation were generated by voxel-by-voxel comparison between each subject's PET SUVR images and a control dataset of 9 healthy individuals. Glial activity load on PET ('GALP') was calculated as the sum of voxel-by-voxel z-scores ≥ 4 in the lesional and perilesional normal-appearing white matter (LWM and P-NAWM), cortical grey matter (CoGM) and thalamic (Th) regions of interest (ROI) in standard atlas space. Mean ROI GALP scores, peripheral CD19 counts, and clinical measurements over 90 days were compared with baseline values. $p < 0.05$ was considered statistically significant.

RESULTS

Mean CoGM-GALP was significantly decreased at 90 days but not at days 5 or 28, post-ofatumumab initiation, as compared to BL (0.75±0.09 vs. 0.93±0.06, -19.4%, $p < 0.05$). Absolute and %CD19 counts were significantly decreased at day 5 vs BL (11.5±9.1 vs. 256.6±117.4 cells/ μ L, -96%, $p = 0.01$ and 0.98±0.98% vs. 14.7±8.7%, -93%, $p = 0.02$), which persisted at day 90. There was no statistically significant difference in mean GALP scores in Th, LWM, and P-NAWM, or in clinical measurements over 90 days (all $p > 0.05$).

CONCLUSIONS

Ofatumumab treatment was associated with decreased CoGM microglial activation at 3 months and was preceded by peripheral CD19+ cell depletion at day 5, which may suggest an indirect, downstream effect of B-cell depletion on microglial activity in RMS patients. Further studies on effects of ofatumumab on microglial activation are warranted.