DOI 10.1007/s00415-006-2001-2

Sixteenth Meeting of the European Neurological Society

27–31 May 2006, Lausanne, Switzerland

Symposia and Free Communications

The abstracts have been reviewed by:
Z. Argov, O. A. Bajenaru, J. Bogousslavsky, O. Combarros, G. Comi, V. Dietz, M. Donaghy, C. Elger, J. M. Ferro, C. Krarup, I. Milonas, G. Moonen, Y. Parman, V. Planté-Bordeneuve, G. Said, E. Scarpini, R. Soffietti, E. Schmutzhard, A. Steck, E. Tolosa, J. Valls-Solé, M. J. D. Vidailhet

Session 14

Multiple sclerosis 4

O106

Myelin basic protein-T cell lines from patients with multiple sclerosis express high affinity full-length BDNF receptor: implications for T-cell survival

L. De Santi, L. Cantalupo, C. Cioni, P. Annunziata
University of Siena (Siena, I)

Objectives: Brain-derived neurotrophic factor (BDNF), a neurotrophin determining neuronal survival during development and repair, is primarily produced by neurons. However, immunocompetent cells, including T cells, produce BDNF in inflammatory lesions of multiple sclerosis (MS) brains, suggesting a role for BDNF in neuroprotective inflammation in MS. To date, there are conflicting data about the ability of immunocompetent cells to express gp145trkB, the high affinity full-length BDNF receptor, in MS. Aim of our study was to evaluate the expression of gp145trkB by CD3 + T lymphocytes, monocytes, lymphoblastoid B cell lines (B-LCLs), myelin basic protein (MBP)-T cell lines from patients with MS and its functional role in MBP-autoreactive T cell line survival.

Material and methods: Peripheral blood mononuclear cells (PBMCs) were obtained from 48 MS patients, 34 with relapsing-remitting (RRMS) and 14 with secondary progressive MS (SPMS) and from 15 sex- and age-matched healthy subjects (HS). T lymphocytes and monocytes were stimulated with phytohemagglutinin (PHA) and interleukin-2 (IL-2), and lipopolysaccharide, respectively. B-LCLs were obtained by Epstein-Barr virus (EBV)-transformed PBMCs. MBP-T cell lines were derived from PBMCs and expanded in vitro upon several cycles of antigen stimulation. gp145trkB protein expression was assessed by western blotting and chemiluminescence assay and related mRNA tested by RT-PCR. To assess the role of BDNF signalling in T cell survival, we analyzed apoptosis in anti-CD3 antibody-stimulated MBP-T cells, in the presence of a neutralizing anti-BDNF antibody and K252a, a gp145trkB inhibitor, by annexin V labeling and fluorescence microscopy.

Results: gp145trkB was expressed by 5 of 34 (15 %) PHA- and IL-2-stimulated CD3 + T cell cultures from RRMS patients. No gp145trkB protein expression was found in monocytes and in T cells from SPMS patients and HS; by contrast, all EBV + B-LCLs and 6 of 9 (67 %) MBP-T cell lines expressed gp145trkB. In anti-CD3-stimulated MBP-T cell lines expressing high affinity full-length BDNF receptor, apoptosis increased by 42 % ($p = 0.03$) in the presence of the neutralizing anti-BDNF antibody and by 66 % ($p = 0.002$) with K252a.

Conclusions: gp145trkB protein expression is a cell-specific and activation-induced process in inflammatory cells in MS. gp145trkB signalling is involved in modulation of peripheral MBP-sensitized T cell line apoptosis, suggesting a regulatory role of T cell line survival.

This work was supported by a grant of the University of Siena to P. A.

O107

Detection of cortical lesions is dependent on choice of slice thickness in patients with multiple sclerosis

O. Dolezal, S. Balachandran, Z. Seidl, M. Vaneckova, C. I. Tekwe, N. Bergsland, M. G. Dwyer, R. Zivadinov
Buffalo Neuroimaging Analysis Center (Buffalo, USA)

Background: Understanding of the importance of cortical lesions in MS pathogenesis has changed. Histopathological studies using new immunohistochemical methods show cortical lesions can be detected more frequently. Newer MRI sequences also detect cortical lesions more accurately.

Objective: To evaluate whether the effect of slice thickness (th) is an important factor for detection of cortical lesions in patients with multiple sclerosis (MS).

Design/Methods: 41 patients with relapsing remitting (RR) MS (11 males, 30 females with mean EDSS 2.3) received FLAIR and 3D-T1-WI of 1.5, 3 and 5 mm slice thickness on 1.5T MRI. Cortical and juxtacortical lesions were volumetrically assessed using a semiautomated method. FLAIR and 3D-T1-WI were co-registered and the matrix of the peripheral gray matter (PGM) segmentation mask (SIENAX-generated) classified the location of the cortical-subcortical lesions. Cortical lesions fell into three classes. Class 1 were defined as lesions located in the PGM, Class 2 as juxtacortical lesions in contact with PGM mask, and Class 3 as cortical-juxtacortical situated in both areas.

Results: Of total T2-lesion volume (LV) measured on 1.5 mm th scans, (mean 16108 cu mm), cortical lesions represented 2.4 % (276 cu mm), juxtacortical lesions 6.1 % (760 cu mm) and cortical-juxtacortical 3.7 %. (491 cu mm). Compared to 1.5 mm th scans, cortical LV was reduced –28.3 %, $p < 0.01$ on 3 mm th and –40.78 %, $p < 0.01$on 5 mm th scans. Results for juxtacortical lesions were: (3 mm th scans:–17.9 %, $p < 0.01$ and –30.3 %, $p < 0.01$ for the 5 mm th scans) and (3 mm th scans: –16.22 %, $p < 0.01$ and –26.7 %, $p < 0.01$ for the 5 mm th scans) for the cortical-juxtacortical lesions.

Conclusions: Lower slice thickness significantly increases detecting accuracy of cortical lesions on FLAIR images. Our results support use of 1.5 mm th for detecting cortical-juxtracortical lesions.

O108

Efficacy of a novel oral single-agent fumarate, BG00012, in patients with relapsing-remitting multiple sclerosis: results of a phase 2 study

L. Kappos, D. H. Miller, D. G. MacManus, R. Gold, E. Havrdova, V. Limmroth, C. Polman, K. Schmierer, T. Yousry, M. Yang, M. Eraksoy, E. Meluzinova, I. Rektor, G. N. O'Neill
Universitätsspital Basel (Basel, CH); University College London (London, UK); University Gottingen and Gemeinnützige Hertie-Stiftung (Gottingen, D); General Teaching Hospital (Prague, CZ); City Hospital of Cologne (Cologne, D); VU Medical Centre (Amsterdam, NL); Biogen Idec (Cambridge, USA); University of Istanbul (Istanbul, TR); Faculty Hospital V Motole (Prague, CZ); Masaryk University (Brno, CZ)

Objective: To determine the efficacy of three dose levels of BG00012, a novel oral fumarate preparation, on brain lesion activity as measured by magnetic resonance imaging (MRI) in patients with relapsing-remitting multiple sclerosis (RRMS).

Methods: This was a randomised, double-blind, placebo-controlled clinical trial of BG00012 in patients with RRMS. Men and women 18 to 55 years of age were eligible for the study if they had a diagnosis of RRMS and an Expanded Disability Status Scale (EDSS) score between 0.0 and 5.0. In addition, patients must have had either ≥ 1 relapse within 12 months prior to randomisation or gadolinium-enhancing (Gd +) lesions on cranial MRI at screening. Patients were assigned to four treatment groups and received BG00012 capsules 120 mg by mouth (PO) once daily (120 mg/day), 120 mg three times daily (360 mg/day), 240 mg three times daily (720 mg/day), or placebo for 24 weeks. The treatment period was followed by a 24-week dose-blinded safety-extension period during which all patients received BG00012. The primary end point was the total number of Gd + lesions over four MRI scans at weeks 12, 16, 20, and 24 (calculated as the sum of the four scans). Secondary end points included the cumulative number of new Gd + lesions from week 4 to week 24 and the number of new/enlarging T2-hyperintense lesions at week 24. Additional end points included the number of new T1-hypointense lesions at week 24, relapse rate, and disability progression as measured by EDSS.

Results: A total of 257 patients were enrolled in the study; 64 patients each were randomly assigned to receive one of the three BG00012 doses and 65 patients to placebo. Approximately 90 % of patients completed the 24-week treatment period. BG00012 (720 mg/day) significantly reduced the mean number of new Gd + lesions (the primary end point) compared with placebo. In addition, BG00012 reduced the cumulative number of new Gd + lesions, the number of new/enlarging T2-hyperintense lesions, and the number of new T1-hypointense lesions compared with placebo.

Conclusion: BG00012 significantly reduces brain lesion activity, in a dose-dependent manner, as measured by MRI in patients with RRMS over 24 weeks of treatment.

This study was sponsored by Biogen Idec and Fumapharm AG.

O109

Phase I/II trial of a MBP encoding DNA plasmid (BHT-3009) alone or combined with atorvastatin for treatment of multiple sclerosis

H. Garren, J. Antel, A. Bar-Or, C. Bodner, D. Campagnolo, J. Gianettoni, F. Jalili, N. Kachuck, Y. Lapierre, M. Niino, J. Oger, M. Price, S. Rhodes, F. Shi, F. Valone, T. Vollmer, L. Weiner, L. Steinman
Bayhill Therapeutics (Palo Alto, USA); Montreal Neurological Inst. (Montreal, CAN); Barrow Neurological Institute (Phoenix, USA); University of Southern California (Los Angeles, USA); University of British Columbia (Vancouver, CAN); Stanford University (Stanford, USA)

Objective: To assess safety and immune modulation by BHT-3009 in MS patients

Background: We have previously shown that DNA plasmids induce antigen-specific immunomodulation in animal models of autoimmune disease. We have begun clinical testing of BHT-3009, a DNA plasmid that expresses full-length human MBP.

Design/methods: We are conducting a 30 patient, randomized, double-blind, placebo-controlled trial in relapsing MS patients. The primary out-