when CBT was assessed against SEGP, WMD was -12.2 (p=0.024) at 4 months, indicating that CBT (individualised therapy) demonstrated significantly better reduction in fatigue compared to SEGP (group therapy). **CONCLUSIONS:** Overall results demonstrated that CBT was significantly superior in alleviating fatigue compared to no therapy, RT, and SEGP. CBT appears to be promising, acceptable and clinically beneficial approach that could potentially benefit patients with MS fatigue in future. Thus, further research is warranted to determine which aspects of CBT are most effective and the optimal delivery of CBT for MS fatigue.

PND3

RELAPSES REQUIRING INTRAVENOUS STEROIDS AND MULTIPLE SCLEROSIS-RELATED HOSPITALIZATIONS: FINDINGS FROM THE PHASE 3 DEFINE AND CONFIRM STUDIES

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OBJECTIVES: To report effects of BG-12 on the reduction in number of relapses requiring intravenous steroids and multiple sclerosis (MS)-related hospitalizations in DEFINE and CONFIRM, two Phase 3 studies of efficacy and safety of oral BG-12 (dimethyl fumarate) in patients with relapsing–remitting MS (RRMS). **METHODS:** Patients aged 18–55 years with RRMS (McDonald criteria 2005) and an Expanded Disability Status Scale score of 0–5.0 were randomized equally to oral BG-12 240 mg twice (BID) or three times daily (TID) or placebo in DEFINE, or to oral BG-12 240 mg BID or TID, placebo, or subcutaneous glatiramer acetate 20 mg/day (reference comparator) in CONFIRM. The primary endpoint at 2 years was: the proportion of patients relapsed in DEFINE, and annualized relapse rate in CONFIRM. Tertiary endpoints in both studies included number of relapses requiring intravenous steroid therapy and MS-related hospitalizations. **RESULTS:** The intent-to-treat populations of the DEFINE and CONFIRM studies comprised 1,234 and 1,417 patients, respectively. In DEFINE, BG-12 reduced the adjusted annualized rate of relapses requiring steroids at 2 years by 52% (BID; rate ratio, 0.48 [95% confidence interval, 0.36–0.63]) and 51% (TID; 0.49 [0.37–0.64]) vs placebo (both p<0.0001). Relative reductions in CONFIRM were 44% (BID; 0.56 [0.42–0.76]) and 49% (TID; 0.51 [0.38–0.70]) vs placebo (p=0.0002 and p<0.0001). BG-12 also reduced the adjusted annualized rate of MS-related hospitalizations at 2 years in DEFINE by 35% (BID; 0.65 [0.41–1.04]) and 45% (TID; 0.55 [0.34–0.88]) vs placebo (p=0.0708 and p=0.0125); relative reductions in CONFIRM were 32% (BID; 0.68 [0.42–1.09]) and 50% (TID; 0.50 [0.30–0.85]) vs placebo (p=0.1092 and p=0.0098). **CONCLUSIONS:** These findings further support the positive efficacy results for the primary and secondary clinical endpoints in DEFINE and CONFIRM, and also suggest potential health economic benefits of BG-12 treatment for relapsing MS.

PND4

CAPSAICIN 8% PATCH MONOTHERAPY FOR TREATMENT OF POST-HERPETIC NEURALGIA: INTEGRATED ANALYSIS OF PHASE III STUDIES

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OBJECTIVES: To demonstrate the clinical effectiveness of capsaicin 8% patch monotherapy in the treatment of post-herpetic neuralgia (PHN) using an integrated analysis of individual patient data from Phase III studies. **METHODS:** Data from four double-blind randomized controlled trials of patches containing either capsaicin 8% w/w (QTZ) or 0.04% capsaicin w/w (CTRL). Study subjects did not use concomitant neuropathic pain medication (either opioid, anticonvulsant, or antidepressant) during study period and received a 60-minute patch application. The primary endpoint was percentage change in numeric pain rating scale (NPRS) "average pain for the past 24 hours" score between Baseline and Weeks 2-8 (week 12 as secondary endpoint) following treatment. The proportion of subjects achieving a 30% decrease in their "average pain" NPRS scores from Baseline to Weeks 2–8 ("Responders") was also analysed. The primary endpoint was analysed with a general linear model with subject baseline characteristics and study allocation entered as fixed effects and trial subgroup entered as a random effect. Statistical significance for all tests was p=0.05. **RESULTS:** A total of 533 subjects received capsaicin monotherapy; 55% received QTZ. QTZ and CTRL subgroups had near-identical baseline characteristics for gender (48% male), age (70.2 years); PHN duration (3.7 years), baseline "average" pain (5.5), and treatment area size (321cm2). The adjusted estimated marginal mean percentage change in pain from Baseline to Week 8 was -36.9% (95% CI: -40.9 to -32.0) for QTZ and -27.3 (-32.0 to -22.7) for CTRL (p=0.001). Baseline to Week 12 percentage change similarly favoured QTZ (p=0.001). At week 8, 52% of QTZ subjects were responders compared with 40% of controls (p=0.007). The adjusted odd-ratio for treatment response was 1.66 (95% CI: 1.15 to 2.40) in favour of QTZ. **CONCLUSIONS:** Capsaicin 8% patch monotherapy is a clinically effective treatment option for post-herpetic neuralgia when compared to low-dose active comparator.

PND5

A MIXED TREATMENT COMPARISON OF GABAPENTIN ENACARBIL, PRAMIPEXOLE, ROPINIROLE AND ROTIGOTINE IN MODERATE-TO-SEVERE RESTLESS LEGS SYNDROME (RLS)

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OBJECTIVES: To compare, in the absence of head-to-head trials, the clinical benefit of gabapentin enacarbil, levodopa, pramipexole, ropinirole, and rotigotine in the treatment of moderate-to-severe restless legs syndrome (RLS). **METHODS:** A mixed treatment comparison (MTC) was performed using the Bayesian approach in the software WinBUGS. A systematic literature review was first conducted to identify RLS trials published over the past ten years through search on MEDLINE, EMBASE, Cochrane CENTRAL and manufacturers' websites. Twenty-eight clinical trials were retained after two screenings. To minimize heterogeneity on dosing and trial duration, a smaller set of fifteen trials were included in the primary analysis, comprising 4,413 patients. A sensitivity analysis was then performed on the full set of twenty-eight trials to validate the results of the primary analysis. **RESULTS:** The indirect comparison was established among four active treatments (gabapentin enacarbil, pramipexole, ropinirole, rotigotine) and placebo, due to the lack of latest clinical evidence on levodopa. Analysis on the primary endpoints indicates that rotigotine is most likely to lead to the greatest reduction in IRLS score from baseline (probability of 64.7% at the end of maintenance, and of 70.6% at week 12). Rotigotine's comparative therapeutic benefit is also observed in IRLS responders rate and in five out of six items of the RLS-6 scale. **CONCLUSIONS:** Based on the results of this MTC, rotigotine is most likely the most efficacious treatment option to alleviate RLS symptoms. Head-to-head clinical trials should be conducted to confirm the findings of this MTC.

PND6

COMBINING RCT AND OBSERVATIONAL DATA IN A MIXED TREATMENT COMPARISON OF DISEASE-MODIFYING-THERAPIES FOR MULTIPLE SCLEROSIS

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OBJECTIVES: The advent of new, costly disease-modifying-therapies (DMT) for multiple sclerosis (MS) requires consideration of all evidence on comparative effectiveness with existing therapies to inform both health policy and clinical care. This study compares the relative effectiveness of DMTs within a mixed treatment comparison (MTC) framework, and explores the contribution of real-world evidence from observational studies to the evidence-base. **METHODS:** Sixteen randomised controlled trials (RCTs) and four observational studies incorporating nine DMTs were identified according to specified inclusion criteria following a systematic review of the literature. A Bayesian MTC model was fitted in WinBUGS, for the outcome Annualised Relapse Rate (ARR). Alternative methods of combining data from different trial designs were used. The model was extended to a meta-regression to include baseline covariates. **RESULTS:** Natalizumab and Fingolimod, two recently approved DMTs, were significantly more effective than other DMTs for the ARR outcome versus placebo, while the least effective option was Interferon beta-1a 6MIU. Minimal differences were observed among the other DMTs. Baseline covariates had no significant impact on the results. Observational data was available only for the older DMTs. An MTC of these trials supported the ranking in effectiveness obtained from the RCT MTC, although individual estimates of effectiveness were different to RCT estimates and uncertainty was substantial. As an alternative to naïve pooling of both RCT and observational data, utilising the observational data as prior information allowed for adjustment of bias due to trial design. **CONCLUSIONS:** Relative clinical effectiveness of DMTs is an important component in the assessment of cost-effectiveness of these agents. RCTs provide the foundation for evaluating comparative effectiveness of DMTs. However, observational studies can contribute complementary evidence on important comparative effectiveness questions.

PND7

OFF-LABEL USE OF ANTIEPILEPTIC DRUGS AND ITS COSTS – A DRUG UTILIZATION STUDY IN PORTUGAL

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OBJECTIVES: This study aimed to analyse the pattern of prescription and use of antiepileptic drugs (AEDs), being its main focuses the characterization of off-label use and its costs. **METHODS:** Cross sectional survey, carried out from Sept. 2009 to Feb. 2010 in 20 pharmacies of Lisbon Region. ***Inclusion criteria***: pharmacy users with a prescription including at least 1 AED (all medicines listed under the Anatomical Therapeutic Chemical code N03-Antiepileptics, having epilepsy in the SPC as main indication). Information was collected by interview, conducted by trained pharmacy students based on self-reported data. Prescription expenditures were obtained by crossing the official price of each medicine single unit, at the time of the study, with data on posology reported by each patient. Aggregate annual expenditures were calculated based on that information. **RESULTS:** Data from 543 patients was analyzed (61.3% females), age range 2-91 years (mean: 50.9). The main consumed AEDs were valproic acid (18.0%), pregabalin (16.2%), topiramate (15.7%) and carbamazepine (14.7%). The first prescriber was in 36.1% of the cases a neurologist and in 31.9% a psychiatrist. Epilepsy was the indication in 29.5% of the patients. Off-label use was found in 33.1% of the sample. Among the off-label sample, topiramate (28.2%), clonazepam (17.2%), valproic acid (16.7%) and gabapentine (10.9%) were the anticonvulsants most widely used off-label. Clonazepam (85.7%) and topiramate (59.0%) had most of their uses in off-label indications. Psychiatrists (59.2%) were the prescribers in the majority of the off-label cases. The main off-label indications were depression (31.4%) and mood stabilization (19.4%). Total costs with AEDs were 210,851.57€ in which 48,424.04€ (23.0%) represents an off-label cost. **CONCLUSIONS:** Approximately 1/3 of the sample used AEDs in off-label indica-