DRUG PERSISTENCE PATTERNS SIMILAR FOR RIVASTIGMINE-TREATED PATIENTS AND DONEPEZIL-TREATED PATIENTS

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OBJECTIVE: To assess "real world" drug persistence patterns for patients with Alzheimer's Disease (AD) treated with clinically effective doses of rivastigmine or donepezil by evaluating rates of discontinuation and change in therapy. METHODS: A retrospective cohort study was conducted using longitudinal pharmacy claims data from the PharMetrics Patient-Centric database. Newly treated, US, community-based AD patients were identified as having an initial prescription (index event) for rivastigmine or donepezil between June and December, 2000. Patients receiving either drug during the 180 days prior to their index prescription or who did not have continuous plan enrollment during this period were excluded. Patients reaching clinically effective doses of donepezil (5``C10 mg/day) or rivastigmine (6``C12 mg/day), and undergoing $\geq$ 60 days continuous therapy were analyzed. The primary outcome measure was time to treatment failure, defined as either discontinuation of therapy (no prescription refill within 90 days of estimated completion of prior prescription) or switch to alternative AD drug. Kaplan-Meier survival and proportional hazard model analyses were performed. RESULTS: A total of 1650 AD patients treated with rivastigmine or donepezil met all study eligibility criteria and reached clinically effective doses. Treatment failure occurred for 66% of donepezil patients (27% within first 60 days) and 60% of rivastigmine patients (20% within first 60 days) during the approximate 1-year follow-up. The mean (95% CI) time to failure was 360 (332``C398) days for the rivastigmine group versus 376 (361``C391) days for donepezil (p = 0.083). In patients receiving the maximum recommended doses, mean time to treatment failure was 392 (372``C412) days with donepezil 10 mg/day versus 403 (352``C454) days for rivastigmine 12 mg/day (p = 0.24). CONCLUSIONS: Drug persistence patterns were similar for rivastigmine and donepezil patients who reach a clinically effective dose, but there was a trend in favor of rivastigmine for patients reaching higher doses.

STANDARD GAMBLE TECHNIQUE—A TOOL TO ASSESS QUALITY OF LIFE IN PATIENTS WITH EPILEPSY

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OBJECTIVE: Epilepsy treatment and associated side-effects have significant impact on patients' health-related quality of life (HRQoL). Literature suggests that generic tools (eg EQ-5D) are not appropriate in epilepsy. This analysis assesses impact on HRQoL of three common anti-epileptic drugs using standard gamble (SG) technique. METHOD: A questionnaire was administered to 65 members of the public without epilepsy (age 18–86) deriving scores for seven health states. Health states corresponded to epilepsy treatment side-effect profiles and associated occurrence probabilities with monotherapy: sodium valproate/VPA [weight gain (30%), hair loss (10%), body hair growth], lamotrigine/LTG [rash (10%)] and carbamazepine/CBZ [lack of concentration (10%), perceived impaired intelligence by others]. Questionnaire for women of childbearing potential/WCBP (aged 18–45) included failure of oral contraception and possibilities of foetal abnormalities (CBZ). Utility scores were derived using standard methodology. RESULTS: Sixty-four respondents completed the exercise: 46 female (17 WCBP), 18 male; average age 51.7 years. None had epilepsy; 10 had a family member with epilepsy. Respondents' utility values [mean (SD)]: 1. Patients controlled: LTG 0.751 (0.300), VPA 0.748 (0.307), CBZ 0.712 (0.338); 2. Patients partially controlled: LTG 0.743 (0.308), VPA 0.706 (0.322), CBZ 0.689 (0.340). Uncontrolled epilepsy (no treatment) was valued at 0.571 (SD 0.380). Utility values for WCBP with partial control were higher for LTG (0.837; SD 0.236) versus CBZ (0.658; SD 0.359) and VPA (0.702; SD 0.314). Utilities for treatments yielding full control were higher than those with partial control. Results are in line with published data on epilepsy. Testing showed no significant differences between respondent sub-groups on any domain. CONCLUSION: Results indicate that both seizure control and treatment side-effects affect utility. SG is a valuable methodology for deriving utilities in epilepsy (compared to generic instruments) for cost-effectiveness analyses (CEA). Applying findings to a decision-tree CEA yielded £13,045/QALY (range £8,928–£18,960) for lamotrigine over sodium valproate and carbamazepine.

FUNCTIONAL ASSESSMENT OF MULTIPLE SCLEROSIS (FAMS): EVALUATING THE LINGUISTIC VALIDITY OF 5 NEW LANGUAGES: PORTUGUESE, JAPANESE, HEBREW, RUSSIAN, AND KOREAN

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OBJECTIVE: To evaluate the performance of newly-translated Portuguese, Japanese, Hebrew, Russian, and Korean FAMS questionnaires. METHODS: Using both qualitative and quantitative data, we assessed the preliminary psychometric properties of the translations. The

translation methodology included two forward translations by native speakers in each language, a reconciled version of the two forwards by a third translator, back-translation of the reconciled version by a native English speaker fluent in the target language, and three independent reviews by native speaking experts. Retrospective debriefing interviews were conducted in which 113 patients (20 in Portugal, 20 in Japan, 19 in Brazil, 34 in Israel, and 20 in Korea) diagnosed with multiple sclerosis were asked to read and answer the questionnaire in Portuguese, Japanese, Hebrew, Russian, or Korean and then give their opinion on any problems with the translation or the content of the questionnaire. Statistical analyses (descriptive statistics and reliability analyses) were performed on the quantitative data, and the participant comments were reviewed. **RESULTS:** Age range was 19 to 64 years; there were 75 women and 38 men. The FAMS performed very well in all target languages. Cronbach's alpha coefficients for total FAMS were high (range = 0.93–0.96), indicating overall scale homogeneity comparable to the original English version. Based upon statistical analyses and comments from patients, no revisions were necessary for the Portuguese, Japanese, Russian, and Korean translations. However, two revisions were made to the Hebrew version as a result of data collected during testing. **CONCLUSIONS:** Participants were comfortable with the questionnaire and felt that the questions addressed issues important to multiple sclerosis. The final versions of the Portuguese, Japanese, Hebrew, Russian, and Korean FAMS are linguistically acceptable and show good psychometric performance, and are now ready for inclusion in clinical trials and other research studies to evaluate the quality of life of patients with multiple sclerosis.

PAIN

PAIN—Clinical Outcomes Studies

TOPIRAMATE FOR THE TREATMENT OF PERIPHERAL DIABETIC NEUROPATHY: CANADIAN CLINICAL EXPERIENCE

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OBJECTIVE: The complexity of peripheral diabetic neuropathy (PDN) and the highly variable effects of individual drugs mean that clinicians continue to seek alternatives for their patients. The objective of this study was to evaluate and describe the use of topiramate for PDN in Canadian clinical practice. **METHODS:** Retrospective review of 100 patient charts using physician interview. Physicians were asked to include the 4 most recent patients that met the following criteria: 1) diagnosis of PDN; 2) topiramate started ≥6 months prior to review date to allow an adequate trial time for drug therapy; 3)

no concomitant gabapentin use. **RESULTS:** Patient characteristics: 8% Type 1 diabetes, 92% Type 2; mean age 55.4 years; 45% male; 85% Caucasian; 61% with medical conditions other than diabetes /PDN requiring drug therapy. Pain distribution: foot/toe 91%, calf 29%, finger/hand 28%, thigh 19%. Pain quality: burning 55%, tingling 47%, pins and needles 30%, aching 23%, sharp 19%, cramping 17%, jabbing 17%, shooting 17%. Topiramate therapy: mean duration 14.4 months; mean total daily dose 136 mg. 98% were current users. Patients had PDN for 21.5 months on average prior to starting topiramate therapy. Topiramate was used as monotherapy in 79%. In 59% topiramate was the first-line drug. 24% experienced topiramate-related adverse effects (AEs); most common: dizziness 29%, somnolence 21%, nausea 17%, and numbness 13%. Actions taken for AEs: none (71%), dose reduction (17%), slower titration (13%), treatment with another drug (4%). According to physician assessment, 64% (95%CI 46, 82) were "very much improved" or "much improved" for pain, 49% (95%CI 30, 68) for physical activity, and 51% (95%CI 33, 70) for sleep. **CONCLUSIONS:** Under conditions of routine clinical care, topiramate was effective in relieving pain and improving physical activity and sleep in patients with PDN. Most patients tolerated the drug long-term with no discontinuation of therapy resulting from AEs.

TOPIRAMATE IS EFFECTIVE IN PATIENTS WITH PERIPHERAL DIABETIC NEUROPATHY FOR WHOM OTHER ANTICONVULSANTS HAVE FAILED

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OBJECTIVE: Neuropathic pain is difficult to manage and pharmacotherapy is often unsatisfactory. Patients often will have tried a large number of drugs in an effort to find relief. This study evaluated the effectiveness and safety of topiramate in patients with peripheral diabetic neuropathy (PDN) who have previously tried other anticonvulsants. **METHODS:** Retrospective review of 100 patient charts using physician interview. Physicians were asked to include the 4 most recent patients that met the following criteria: 1) diagnosis of PDN; 2) topiramate started ≥6 months prior to review date to allow an adequate trial time for drug therapy; 3) no concomitant gabapentin use. A subgroup of 28 patients that had failed other anticonvulsants prior to topiramate was analyzed. **RESULTS:** Patient characteristics: 14% Type 1 diabetes, 86% Type 2; mean age 64.9 years; 54% males; 93% Caucasian. Most commonly affected areas: foot/toe (82%), calf (36%), finger/hand (32%), thigh (21%). Most common qualities: burning (57%), tingling (50%), aching (46%), pins and needles (21%). Previous anticonvulsants included gabapentin (82%), carbamazepine (29%), clonazepam (4%), and divalproex (4%). The most common