

Commission on Medical Therapies

Patrick Kwan, Chair

The Commission on Medical Therapies (Patrick Kwan, Australia, Chair) is involved with seven different aspects related to the treatment of patients with epilepsy. Its mission has always been to improve the care of patients with epilepsy by facilitating collaboration among clinicians, scientists

and other professionals. The Commission has a broad mandate to review current treatments, and to advocate for improvements related to drug therapies and other non-surgical interventions. Its seven areas of activity include AED trials and regulatory affairs (Jackie French, Chair), dietary therapy (Eric Kossoff, Chair), the use of natural products and botanicals (Steve Schachter, Chair), efficacy outcomes (Mark Cook, Chair), emergency treatments (Eugen Trinka, Chair), Emergency treatments (Eugen Trinka, Chair) and psychobehavioral therapy (Rosa Michaelis and Markus Reuber, Co-chairs).

The AED Trials and Regulatory Affairs Task Force worked on three targeted areas. The first was to harmonize the extrapolation of efficacy in adult add-on trials in focal seizures to the pediatric age group. The EMA had already accepted that drugs that are approved in adults for add-on therapy of focal epilepsy should also be approved in children down to the age of two. The PEACE initiative (Pediatric Extrapolation Academic Consortium in Epilepsy), a group led by Jack Pellock, submitted a white paper that suggested a similar extrapolation for FDA approvals. This effort was also a part of the FDA critical path. As a result



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of these efforts, the FDA has accepted extrapolation down to the age of four. This is a momentous decision, based on a substantial PK/PD modeling effort. As a result, new drugs will reach pediatric patients faster and fewer children will need to be exposed to placebo in clinical trials. The second area of activity was to facilitate monotherapy approvals. The Task Force submitted a white paper to the FDA suggesting that drugs should be approved for indications (e.g., focal epilepsy, Lennox-Gastaut syndrome) for both monotherapy and polytherapy use, irrespective of the way the trials were performed (i.e. as monotherapy or polytherapy). A paper was subsequently published in *Lancet Neurology* supporting the arguments in the white paper (Mintzer, French et al. Is a separate monotherapy indication warranted for antiepileptic drugs? 2015 *Lancet Neurology*, 14: 1229–40). The FDA is considering the arguments. The final topic concerned using time to event as a new approach to clinical AED trials. Drs. French and Bagiella have accumulated evidence suggesting that regulatory studies can be performed using time to event rather than parallel arm designs. This would shorten placebo exposure times. The FDA and EMA are considering the approach.

The Botanicals Task Force has finalized the content of “Epilepsy Naturapedia,” a wiki, to be hosted on the ILAE website, which will be the most comprehensive, current and customizable central research hub for bench- to bedside scientific information on the use of natural products for the treatment of epilepsy. Among its many features, Epilepsy Naturapedia enables users to search for information using common names, scientific names and names of compounds. Visitors may also search for names of historical neurologists, historical use, pharmaceutical information and any published evidence for use in the treatment of epilepsy.

The Dietary Therapy Task Force published a monograph in *Epilepsia* (Kossoff et al, What are the minimum requirements for ketogenic diet services in resource-limited regions? Recommendations from the International League Against Epilepsy Task Force for Dietary Therapy 2015, 56:1337–42). The Task Force also maintains a webpage: <http://www.ilae.org/Commission/medther/keto-index.cfm>.

The Psychobehavioral Therapy Task Force is working to update Cochrane reviews of psychological treatments for people with epilepsy, with a focus on health-related quality of life. The literature search and risk of bias evaluation of identified studies has been concluded. This Task Force is also creating treatment recommendations on psychological management for adults and children with epilepsy based on Cochrane reviews, systematic review and the clinical experience. Key intervention strategies and components will be presented as they seem suitable to address various treatment targets that arise in epilepsy. A detailed description of the intervention elements will be published in a glossary as supplementary material online. A brief overview of treatment modalities including options for resource-poor settings, service evaluation measures, and implications for training and facilities offering psychological services for people with epilepsy is provided. To increase comparability and reproducibility of future studies, the inclusion of outlined key intervention elements should be clearly referenced and the standard use of the QOLIE-31 as primary or secondary outcome parameter is recommended.