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Nigel Tan (Singapore)

Psychobehavioral Therapy:
Rosa Michaelis (Germany), Co-chair
Markus Reuber (UK), Co-chair
Laura Goldstein (UK)
William C. LaFrance Jr. (USA)
Avani Modi (USA)
David Rosenstein (Africa)
Venus Tang (Hong Kong)
Janelle Wagner (USA)

Aims

To complete efforts begun by the previous commission and to define and pursue opportunities for progress consistent with the ILAE Strategic Plan in several key therapy-related areas. Significant progress has been made in several projects, which are reported below.

AED Trials and Regulatory Affairs Task Force

This year we continued to work on three targeted areas:

1. Harmonization on extrapolation of efficacy determined in adult add-on trials in focal seizures to the pediatric age group. The EMA had already accepted that drugs approved in adults for add-on therapy of focal epilepsy should also be approved in children down to the age of 2. 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 of these efforts, the

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FDA has accepted extrapolation down to the age of 4. 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.

2. 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 S*, French J*, Perucca E, Cramer J; Messenheimer J, Blum D, Rogawsk M, Baulac M. [*shared first authors] Is a separate monotherapy indication warranted for antiepileptic drugs? 2015 Lancet Neurology, 14: 1229–40). The FDA is considering the arguments.
3. Time to event: Drs. French and Bagiella have accumulated evidence to write a white paper suggesting that regulatory studies can be performed as time to event rather than parallel studies. This would shorten placebo exposure times. The FDA and EMA are considering the approach.

Plans for the Future

A meeting is in preparation in conjunction with the Prague European Congress of Epilepsy, during which FDA, EMA and PMDA will continue to discuss the issues above.

Botanicals Task Force

The task force has finalized the content of the "Epilepsy Naturapedia," a wiki to be hosted on the ILAE website, that 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. The actual launch of the website is being planned. Among its many features, Epilepsy Naturapedia enables users to search for information using:

1. Common names
2. Scientific names
3. Names of compounds
4. Names of historical neurologists
5. Historical use
6. Pharmaceutical information
7. Published evidence for use in the treatment of epilepsy.

Dietary Therapy Task Force

After the meeting in Liverpool in October 2014, we were able to write our proceedings into a manuscript and it was published in *Epilepsia*. The full reference is: Kossoff EH, Al Macki N, Cervenka MC, Kim HD, Liao J, Megaw K, Nathan JK, Raimann X, Rivera R, Wiemer-Kruel A, Williams E, Zupec-Kania B. 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. *Epilepsia*. 2015 Sep;56(9):1337-42.

We also have continually updated our task force Ketogenic Diet webpage:

http://www.ilae.org/Commission/medther/keto-index.cfm

Psychobehavioral Therapy Task Force

In 2015 the task force met two times during the ILAE meeting in Istanbul and the AES meeting in Philadelphia to work on two goals:

1) Update Cochrane review of psychological treatments for people with epilepsy with a focus on HRQOL: By the end of 2015 the literature search and risk of bias evaluation of identified studies have been concluded. The review protocol will soon be published on Cochrane.org after which the data analysis will be conducted. We plan to publish the final results in *Epilepsia* after online publication on Cochrane.org.

2) Create treatment recommendations on psychological management for adults in children with epilepsy based on Cochrane review, systematic review (Tang et al. 2014) and the clinical experience represented by the experts in this task force: A first draft of these recommendations is structured as follows: Key intervention strategies and components are presented as they seem suitable to address various treatment targets that arise across the illness trajectory 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

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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.