8 weeks Randomized Controlled Trial of topiramte vs placebo in patients with Prader Willy Syndrom for behavioural disorders including hyperphagia, irritability/impulsivity and self-injury.

TOPRADER

- Grant of Ministry of Health n° AOM 10088
- Multicenter study : Paris, Toulouse, Hendaye. 2 years inclusion.
- Leading Investigator, Pr Olivier Bonnot, University of Nantes
- Co-Investigators : Pr Maithé Tauber, University Sabatier of Toulouse; Dr Denise Thuilleaux, Hôpital Marin d'Hendaye; Dr Consoli, Center for Rare Disease with Psychiatric Symptoms, Pitié-Salpétrière Hospital, Paris.

Background :

Prader Willi Syndrom (PWS) is a rare genetic disease involving 15 q11-q13 area. Symptoms encompass a severe obesity, hypotonic state, which could lead to death, a intellectual deficiency from mild to moderate, a delayed growth and hypogonadism. Psychiatric and behavioural symptoms are common and represent a major issue : (i) oppositional and defiant disorders with irritability and impulsivity; (ii) self injury behaviours and, (iii) eating disorders with hyperphagia more addictive type.

There is no specific treatment of endocrine impairment involved in PWS. Regarding psychiatric symptoms, antipsychotics are the common medication. Unfortunately they are not highly efficient and moreover their major side effect is weight gain. An alternate medication option is topiramate. It is an antiepileptic, also used for long as thymoregulator and anti-impulsive medication. Interestingly, topiramate is used in eating disorders to loose weight by lowering hunger (PWS patients never feel satiety).

Literature in PWS and topriramate is very scares, there are few case report and on open label study (n=8). This few data, and experience in specialized centre are encouraging. There is to date no RCT in this field.

Objective

Primary: To evaluate efficiency of topiramate (200 mg : day) on irritability and impulsivity (I), self injury behaviours (S) and eating disorders (E) in PWS patients.

Secondary : To evaluate tolerance of topiramate (200 mg : day) specifically on metabolic status and psychiatric symptoms

Methodology

It is a multicentre RCT topiramate versus placebo on 8 weeks. Patients (n=125) have a molecular diagnose of PWS with one at least of the 3 behavioural symptoms: I, S or E. They are randomized in two group, one with placebo and second with a titration of 50mg topiramate first week to 200 at week 5 (50mg raise every week). We have to sample, one with inpatients in a specialized care unit (n=56, Hendaye) and one with outpatient (n=56).

Main evaluation criterion is Global Improvement Scale (GIF), responding patient should have 1 or two at GIF after 8 weeks.

Secondary evaluation criteria are weight, BMI, self-Injury, Nisonger, Dickens, BPRS scales.