SYNOPSIS

Name of Sponsor/Company:	Johnson & Johnson Pharmaceutical Research & Development, L.L.C.	
Name of Finished Product:	TOPAMAX® (topiramate)	
Name of Active Ingredient(s):	2,3:4,5-Di-*O*-isopropylidene-β-D-fructopyranose sulfamate	

Protocol No.: TOPMAT-OBE-3001 (CR003409)

Title of Study: A Study to Explore the Mode of Action of Topiramate in the Treatment of Obese Subjects With and Without Type 2 Diabetes Mellitus Using DNA Samples From Subjects Who Were Randomized Within Select Previous Topiramate Obesity and Diabetes Studies

Principal Investigator: Lars Sjoestroem, M.D., Ph.D., Sahlgrenska Universitetssjukhuset, Goteborg, Sweden

Publication (Reference): None

Study Period: 06 May 2004 to 28 April 2005	**Phase of development:** 3

Objectives: The primary objective of this study was to explore the mode of action of topiramate in the treatment of obese and diabetic subjects by testing the association between genetic polymorphisms within candidate genes and chromosomal regions and the clinical endpoints of percent change in weight, change in hemoglobin A_{1c} (HbA_{1c}), and central nervous system (CNS)-related adverse events. For this purpose, the study aimed to analyze genetic polymorphisms in the DNA extracted from blood samples collected from subjects who were randomized within selected previous topiramate obesity and diabetes studies.

Safety was assessed for all subjects.

Methodology: This was a pharmacogenomics study that required collection of a single 10-mL blood sample for genetic analyses. No study drug was administered. The results of the genetic analyses will be used in conjunction with results of data collected from previous topiramate obesity and diabetes studies.

Subjects who were randomized in the TOPMAT-OBES-002 (PRI/TOP-INT-31) or TOPMAT-OBDM-003 (PRE/TOP-INT-33) clinical studies, as well as a subset* of subjects with diabetes mellitus who were randomized within the TOPMAT-OBDM-002 (PRI/TOP-INT-34) study, were eligible to participate. All subjects signed an informed consent within 7 days of sample collection that indicated they understood the purpose of the study and the required procedures. Subjects who had received a blood transfusion within 60 days before the blood sample collection were excluded from the study. The study consisted of a screening telephone contact, a single visit to the study center for a blood sample collection, and a 24-hour post-sample adverse event reporting period

Number of Subjects (planned and analyzed): A subject was considered as having completed the study if a blood sample for DNA analysis had been collected. A total of 1144 of the 1145 subjects who were screened for the study provided blood samples for DNA analyses. Of the 1144 subjects enrolled in this study, 801, 269, and 74 subjects had been enrolled within selected previous topiramate obesity and diabetes studies TOPMAT-OBES-002 (PRI/TOP-INT-31), TOPMAT-OBDM-003 (PRE/TOP-INT-33), and TOPMAT-OBDM-002 (PRI/TOP-INT-34), respectively.

Diagnosis and Main Criteria for Inclusion: Pariticipation in prior topiramate obesity and diabetes studies.

Test Product, Dose and Mode of Administration, Batch No.: No study drug administered

SYNOPSIS (CONTINUED)

Reference Therapy, Dose and Mode of Administration, Batch No.: NA

Duration of Treatment: NA

Criteria for Evaluation: This was a pharmacogenomics study that required collection of a single 10-mL blood sample for genetic analyses. No study drug was administered. The results of the genetic analyses will be used in conjunction with results of data collected from previous topiramate obesity and diabetes studies.

Statistical Methods: Clinical data from subjects randomized within the select previous topiramate obesity and diabetes studies will be merged with their genotype data and 2 types of analyses will be performed: a candidate gene analysis and a genome screen.

SUMMARY - CONCLUSIONS

SAFETY RESULTS: Two subjects experienced a treatment-emergent adverse event after the blood sample collection on Day 1 (Table 3). Subject 1001 experienced a moderate haemorrhage, and Subject 1002 experienced a mild haematoma. Both events were considered very likely related to the venipuncture and resolved without any concomitant therapy intervention.

PHARMACOGENOMICS: A single blood sample was collected for genetic analyses from a total of 1144 subjects who had been randomized within the TOPMAT-OBES-002 (PRI/TOP-INT-31), TOPMAT-OBDM-003 (PRI/TOP-INT-33), and a subset of subset of subjects with diabetes mellitus within the TOMAT-OBDM-002 (PRI/TOP-INT-34) studies. PG data not yet available.

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