These results are supplied for informational purposes only.
Prescribing decisions should be made based on the approved package insert in the country of prescription

Sponsor/company:	sanofi-aventis	**ClinialTrials.gov Identifier:**	NCT000477373
		Study Code:	DPKOT_L_01567
Generic drug name:	Di-Valproate	**Date:**	18/Dec/2008

Title of the study:	A multicenter, phase IV, non-comparative, open study of a flexible dose of valproate to assess the efficacy of valproate in Bipolar I patients suffering from a manic episode according to DSM IV (APA 1994) over a 12 weeks period of treatment. **Gulf Evaluation of VAlproate in maNia Study— *GEVANS*—**. Study code: DPKOT_L_01567		
Investigator(s):	**Dr Adel ALZIED** (consultant psychiatrist –Psychiatric hospital-Kuwait).		
Study center(s):	8 centers in 4 countries (Kuwait, Qatar, Bahrain & Oman)		
Study period: Date first patient enrolled: 01-Dec-2006 Date last patient completed: 31-Dec-2007	**Phase of development:** Phase. IV		
Objectives:	**Primary Objective:** To assess the efficacy of valproate in Bipolar I patients suffering from a manic episode according to DSM IV (APA 1994) over a 12 weeks period of treatment.. **Secondary Objective:** To evaluate the clinical safety of valproate.		
Methodology:	A multicenter, phase IV, non-comparative, open study of a flexible dose of valproate**.**		
Number of patients:	Planned: 100	Enrolled: 70	Treated: 70
Evaluated:	Efficacy: 70	Safety: 70	
Diagnosis and criteria for inclusion:	• In or out patients of either sex • Patients aged 18 to 75 years inclusive • Patients able to comply with the protocol • Patients having given their written informed consent • Patients with a current diagnosis of Bipolar I Disorder according to DSM IV (296) • Patients suffering from a current manic episode or mixed episode		
Investigational product: Dose/ Administration:	Valproate: available tablets of Depakine Chrono 500 mg If the daily dose does not exceed 1000 mg, Depakine CHRONO can be administered once a day. If the dose is greater than 1000 mg/day, Depakine CHRONO will be administered in a bid regimen: one tablet in the morning and one tablet in the evening. The higher dose should be given the evening. The dosage will be adjusted according to the Clinician judgment.		
Duration of treatment: 12 weeks	**Duration of observation:** 12 weeks		
Criteria for evaluation:			
Efficacy/Pharmacodynamics:	The primary criterion used to assess the efficacy will be based on the Clinical Global Impressions Scale for Bipolar Disorder (CGI-BP) [10]. The mean change in the CGI-BP Severity score between D0 and D21 and D0 and D END will be analyzed.		

Safety:	Vital parameters : - Systolic and diastolic blood pressure and heart rate in supine and standing positions - Body weight
Statistical methods:	Descriptive analysis was used : ➢ *Repeated Measures Analysis of Variance* ➢ Friedman Test (Non-parametric Repeated Measures ANOVA)

Summary:

Significant reduction in severity of both Mania & depression from Baseline till day 21st and from baseline till day 84 (study end) with P value <0.05

Friedman Test (Nonparametric Repeated Measures ANOVA)

The P value is < 0.0001, considered extremely significant.

Variation among column medians is significantly greater than expected by chance.

Calculation detail:

Group	*Sum of Ranks*
Mania bsl	*220.00*
Mania D21	*184.00*
Mania D42	*122.00*
Mania D84	*84.000*

Friedman Test (Nonparametric Repeated Measures ANOVA)

The P value is 0.0051, considered very significant. Variation among column medians is significantly greater than expected by chance.

Calculation detail: Number of Rows = 26; Number of columns = 4; Friedman Statistic Fr = 12.808 (corrected for ties)

Group	Sum of Ranks
Depress BsL	73.500
Depress D21	74.500
Depress D42	60.000
Depress D84	52.000

Safety results:

1. No change in Blood pressure or vital signs between Baseline & Day 21st or baseline & day 84 or 42.
2. In term of adverse events, the following tabulation summarises the results:

At Baseline:

Side Effects	Count	%
Yes	5	7.14%
No	64	91.43%
Missing	1	1.43%
Grand Total	**70**	**100.00%**

Side Effect	Severity	Count	%
Headache	Mild	1	20.00%
Nausea	Mild	1	20.00%
Nausea + Gastric Irritation	Moderate	1	20.00%
Weight gain	Mild	2	40.00%
		5	**100.00%**

At D21:

Side Effects D21	Count	%
Yes	8	11.43%
No	61	87.14%
(blank)	1	1.43%
Grand Total	**70**	**100.00%**

Side effect 1	Severity	Side effect 2	Severity	If Pt is Unreliable	Count	%
Hair Loss	Mild				1	12.50%
Nausea	Mild	Skin rashes	Mild		1	12.50%
	Mild				1	12.50%
Sedation	Mild				1	12.50%
Weight Gain	Mild				3	37.50%
	Moderate			Non-Study Medication added	1	12.50%
					8	**100.00%**

At D42:

Side Effects D42	Count	%
Yes	5	7.14%
Missing	1	1.43%
No	61	87.14%
(blank)	3	4.29%
Grand Total	**70**	**100.00%**

Safety results:	

Side effect	Severity	If Pt is Unreliable	Count	%
Hair Loss	Moderate		1	20.00%
Increase Body Weight	Mild		1	20.00%
Sedation	Mild		1	20.00%
Weight Gain	Moderate	Non-Study Medication added	1	20.00%
			1	20.00%
			5	**100.00%**

At D84:

Side Effects D84	Count	%
Yes	1	1.43%
No	60	85.71%
(blank)	9	12.86%
Grand Total	**70**	**100.00%**

Specify 1 D84	Inconvenience	Count	%
Increase Body Weight	Mild	1	100.00%

Date of report:	27-November- 2008