



**A CLINICAL STUDY TO EVALUATE THE EFFICACY & SAFETY OF INSTAVIT®  
INSTANT ENERGY ORAL SPRAY IN THE IMPLICATIONS ON HEALTH AND  
PERFORMANCE ON EVERYDAY FATIGUE CONDITION AND IMPROVEMENT OF  
ALERTNESS**

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Article Received on 22/09/2018

Article Revised on 12/10/2018

Article Accepted on 01/11/2018

**ABSTRACT**

**Background:** NEW Instavit® instant energy is a doctor formulated oral spray supplement contains an ideal blend of caffeine and B vitamins to help improve alertness and fight everyday fatigue. **Energy** is power that may be translated into motion, overcoming resistance or causing a physical change; the ability to do work. **Fatigue** (also called exhaustion, tiredness, languidness, languor, lassitude, and listlessness) is a subjective feeling of tiredness which is distinct from weakness, and has a gradual onset. **Alertness** is the state of active attention by high sensory awareness such as being watchful and prompt to meet danger or emergency, or being quick to perceive and act. **Objectives:** The aim of the study is to evaluate the safety and efficacy of Instavit® instant energy oral spray in the implications on health and performance on everyday fatigue condition and improvement of alertness. **Conclusion:** Considering the results and outcomes of all the primary and secondary end-points it is clearly evident that Instavit® instant energy oral spray is more efficacious than Placebo-A in alleviating the fatigue and improving alertness in day to day life. As per the study outcomes no serious and / or moderate adverse events were observed during the clinical trial. So, this proves that Instavit® instant energy oral spray is more safe, efficient and superior in comparison to Placebo-A for implications on health and performance on everyday fatigue condition and improvement of alertness.

**KEYWORDS:** Fatigue, Niacin and Vitamin B12.

**INTRODUCTION**

**Energy** is power that may be translated into motion, overcoming resistance or causing a physical change; the ability to do work. All activities of the body require energy, and all needs are met by the consumption of food containing energy in chemical form. The human diet comprises three main sources of energy: carbohydrates, proteins, and fats. Of these three, carbohydrates most readily provide the kind of energy needed to activate muscles. Proteins work to build and restore body tissue.

**Fatigue** (also called exhaustion, tiredness, languidness, languor, lassitude, and listlessness) is a subjective feeling of tiredness which is distinct from weakness, and has a gradual onset. Unlike weakness, fatigue can be alleviated by periods of rest. Fatigue can have physical or mental causes. Physical fatigue is the transient inability of a muscle to maintain optimal physical performance, and is made more severe by intense physical exercise. Mental fatigue is a transient decrease in maximal cognitive performance resulting from prolonged periods of

cognitive activity. It can manifest as somnolence, lethargy, or directed attention fatigue.

Medically, fatigue is a non-specific symptom, which means that it has many possible causes and accompanies many different conditions. Fatigue is considered a symptom, rather than a sign because it is a subjective feeling reported by the patient, rather than an objective one that can be observed by others. Fatigue and 'feelings of fatigue' are often confused.

Fatigue is a normal result of working, mental stress, overstimulation and under stimulation, jet lag or active recreation, depression, and also boredom, disease and lack of sleep. It may also have chemical causes, such as poisoning or mineral or vitamin deficiencies. Chronic blood loss frequently results in fatigue, as do other conditions that cause anemia. Fatigue is different from drowsiness, where a patient feels that sleep is required. Fatigue is a normal response to physical exertion or stress, but can also be a sign of a physical disorder.

Temporary fatigue is likely to be a minor illness like the common cold as one part of the sickness behavior response that happens when the immune system fights an infection.

**Alertness** is the state of active attention by high sensory awareness such as being watchful and prompt to meet danger or emergency, or being quick to perceive and act. It is related to psychology as well as to physiology. A lack of alertness is a symptom of a number of conditions, including narcolepsy, attention deficit disorder, chronic fatigue syndrome, depression, Addison's disease, or sleep deprivation. Pronounced lack of alertness can be graded as an altered level of consciousness

#### Description

NEW Instavit<sup>®</sup> instant energy is a doctor formulated oral spray supplement contains an ideal blend of caffeine and B vitamins to help improve alertness and fight everyday fatigue.\* Get the energy boost you need when you need it!

- No sugar crash.
- Zero sugar, zero calorie oral spray supplement.
- Pure. Potent. Portable.
- 28 doses per bottle.

#### Ingredient

Niacin and Vitamin B12 (as cyanocobalamin, Methylcobalamin, coenzyme 12)

#### Proprietary Blend

Caffeine, Glucuronolactone, N-acetyl-L-Tyrosine, L-Arginine alpha- Ketoglutarate.

**Other Ingredients:** Purified Water, Vegetable Glycerin, Natural Flavors, Polysorbate 20, Citric Acid, Sucralose, Acesulfame Potassium, Xanthan Gum, Potassium Sorbate (Preservative), Sodium Benzoate (Preservative), and Licorice Root Extract.

Vitamin B12 functions as a coenzyme, meaning that its presence is required for enzyme-catalyzed reactions.

Niacin and niacinamide are indicated for prevention and treatment of vitamin B3 deficiency states. Vitamin B3 (Niacin) also acts to reduce LDL cholesterol, triglycerides, and HDL cholesterol.

#### OBJECTIVES

##### Primary Objective

To assess the efficacy of Instavit<sup>®</sup> instant energy oral spray in the implications on health and performance on everyday fatigue condition and improvement of alertness.

##### Secondary Objective

To evaluate the safety of Instavit<sup>®</sup> instant energy oral spray in the implications on health and performance on everyday fatigue condition and improvement of alertness.

#### METHODS

##### Inclusion Criteria

Healthy male and female between ages 18-60 years, have the willingness to undergo treatment of everyday fatigue condition and improvement of alertness. Subjects meet the BMI between 20.0 – 25.9 kg/m<sup>2</sup>. Subject meet criteria for fatigue as per Chalder Fatigue Assessment scale. Subjects able to comply with all trial requirements were included in the study and willing to provide written informed consent for participation in the study and adhere to the protocol requirements.

##### Exclusion Criteria

Subjects having a medical history of significant hypersensitivity or allergic reaction to any of the active or inactive ingredients. Subjects having history of drug or alcohol abuse, medical history of HIV, HAV, HBsAg, psychiatric illness and Hearing or memory impairments. Pregnant or lactating women and Volunteers who have participated in any drug research study within past 3 months will be excluded from the study.

Study was conducted by randomized, Double Blind, parallel group, placebo controlled clinical study by ICBio Clinical Research Pvt. Ltd. It involved in the clinical attendance of the subjects on recruitment and on follow –up. Subjects enrolled in the study received Study drug (from Baseline visit to EOT-28 days – Instavit<sup>®</sup> instant energy oral spray.

The safety and efficacy parameters were compared with baseline and follow-up data with laboratory investigations, demographics were analyzed in the study. Adverse events / side effects were noted for each follow-up visits.

##### Ethics Committee Approval

All study related documents Protocol, Case Report Form, Dairy card, Investigator Brochure and Informed Consent Documents (English and Kannada Versions). Written Informed Consent was obtained from the subjects before the start of the trial and after due approval from IEC/IRB. Ethics Committee notifications as per the GCP guidelines issued by Central Drugs Standard Control Organization and Ethical guidelines for biomedical research on human subjects issued by Indian council of Medical Research has been followed during the Conduct of the Study (Sapthagiri Institute of Medical Science & Research Centre and Approved on 30 Aug 2017).

##### Study Outcomes

###### Primary Outcomes

- Improvement in fatigue level by using Fatigue assessment test
- Changes in severity of fatigue by using Fatigue Severity scale
- Improvement in overall condition by assessing the Changes in Piper fatigue scale from baseline to EOT.

**Secondary Outcomes**

- Assessment of energy level by using Ergometer for instant energy.
- Changes in Chalder Fatigue Assessment scale.
- Incidence and Rate of adverse events.

**Disposition of Subjects**

Total of 50 subjects

Drug A: Instavit® Instant energy oral spray (25 subjects)

Drug B: Placebo (25 subjects)

**Visit Details**

The patients were screened and enrolled. The enrollment day was considered as the baseline Day and the patient were follow up till end of treatment visit on Day 37.

**Data Sets Analyzed****Table 1: Data sets analyzed for the test and placebo treatments.**

Treatments	Placebo	Investigational Product
Enrolled	25	25
Randomized	25	25
No. of patients completed visit	25	25
Withdrawn	0	0

**Efficacy Evaluation****Primary Endpoints**

Primary endpoints consideration were Improvement in fatigue level, Changes in severity of fatigue, Improvement in overall condition by assessing the fatigue scale from baseline to EOT. Efficacy evaluation was done based on both Primary and secondary endpoints considered in the trial. All the information

**Statistical Analysis**

Data Analysis was carried out using 5% significance level and 80% power for study using SAS. The difference within the group will be assessed using paired t-test.

**RESULTS**

In the study 50 patients were screened and enrolled after meeting the inclusion Criteria and they are Randomized randomly into Drug A and Drug B. The enrolled subjects consisted of Healthy male and Female.

regarding the Fatigue was captured in the Fatigue assessment test, Fatigue Severity scale, Piper fatigue scale respectively. It was done in-order to get the exact estimate of the improvement in energy and fatigue of the patients from baseline to EOT. A descriptive demonstration on the efficacy evaluation for all the above mentioned are presented below

**Demographic data of the study subjects by sex**

Drug Code	Female	Male	Total subject in each drug group
A	14	11	25
B	10	15	25
Total	24	26	50

**Table 2a: Demographic data of the study subjects by Highest Level of Education.**

Table of Drug Code by Highest level of education						
Drug Code	Highest level of education					Total
Frequency	High school	Intermediate (2 year college)	Less than high school	Masters	Professional degrees	Total
A	8	7	2	0	8	25
B	15	8	1	1	0	25
Total	23	15	3	1	8	50

**Table 2b: Demographic data of the study subjects by relatives with any disease.**

Table of Drug Code by Do you have any relatives with any of diseases?				
Drug Code	Do you have any relatives with any of diseases?			Total
Frequency	Diabetes	High blood pressure	Nil	Total
A	3	0	22	25
B	3	1	21	25
Total	6	1	43	50

Table 3: Descriptive statistics of Demographic data.

Drug Code	STATISTICS	Age (in Years)	Weight (in Kg)	Height (in Mt.)	BMI
A	N	25	25	25	25
	MIN	20	48	1.48	20.264
	MAX	57	77	1.78	24.965
	MEAN	35.32	58.9	1.604	22.793
	STD	10.711	7.700	0.075	1.366
B	N	25	25	25	25
	MIN	18	50	1.43	20.546
	MAX	52	70	1.751	25.431
	MEAN	36.72	58.8	1.608	22.731
	STD	10.876	6.300	0.085	1.483

## Efficacy analysis for primary end-points

## 1. Improvement in fatigue level by using Fatigue assessment test

Table 4		
I am bothered by fatigue		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	16.76	<.0001
Test-B	20.72	<.0001

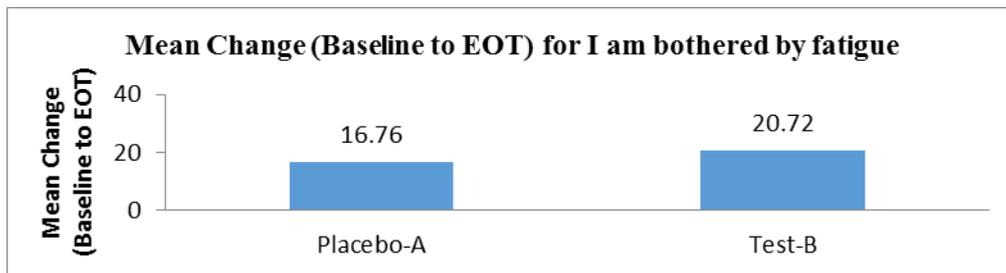


Fig. 1

Table 5		
I get tired very quickly		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	17.64	<.0001
Test-B	21.64	<.0001

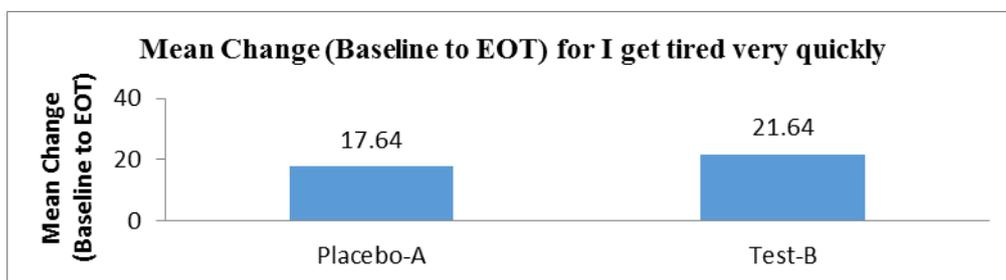


Fig.2

Table 6		
I don't do much during the day		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	12.24	<.0001
Test-B	13.80	0.0002

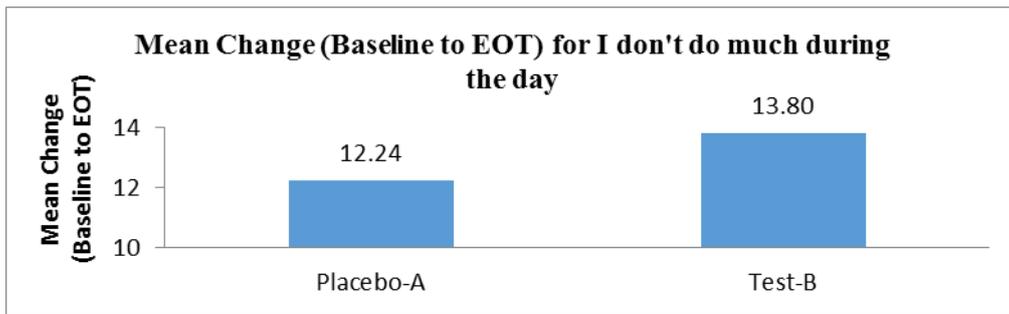


Fig. 3

Table 7		
I have enough energy for everyday life		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	8.56	0.0165
Test-B	17.60	<.0001

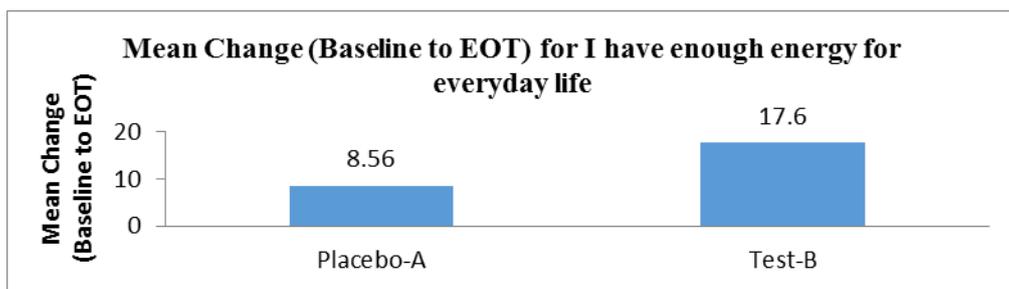


Fig. 4

Table 8		
Physically, I feel exhausted		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	16.88	<.0001
Test-B	21.00	<.0001

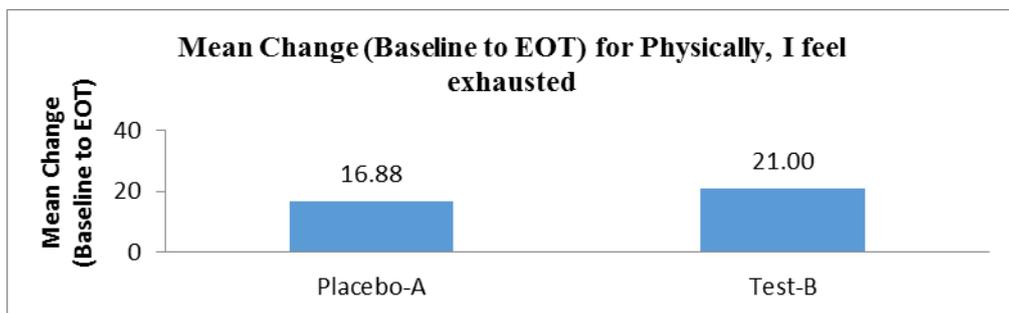


Fig. 5

Table 9		
I have problems to start things		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	17.24	<.0001
Test-B	19.60	<.0001

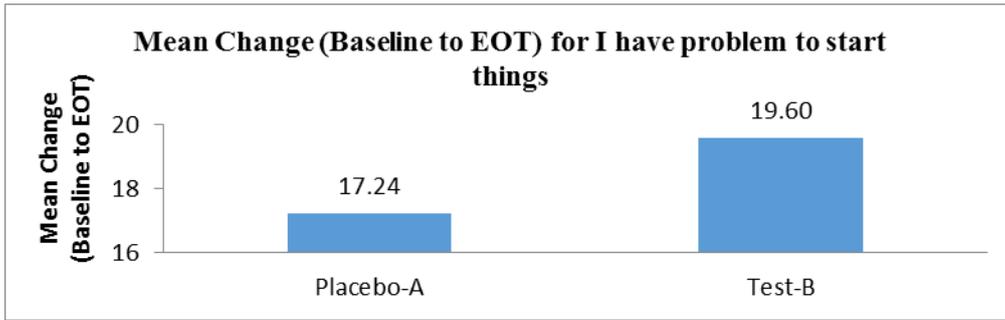


Fig.6

Table 10		
I have problems to think clearly		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	20.32	<.0001
Test-B	20.40	<.0001

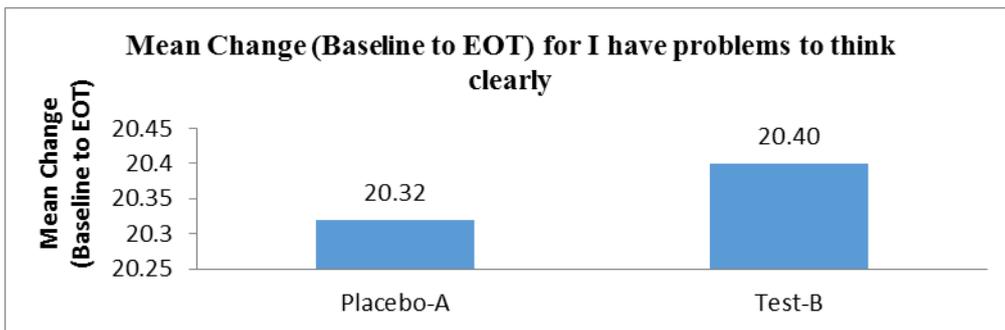


Fig. 7

Table 11		
I feel no desire to do anything		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	15.36	0.0002
Test-B	22.40	<.0001

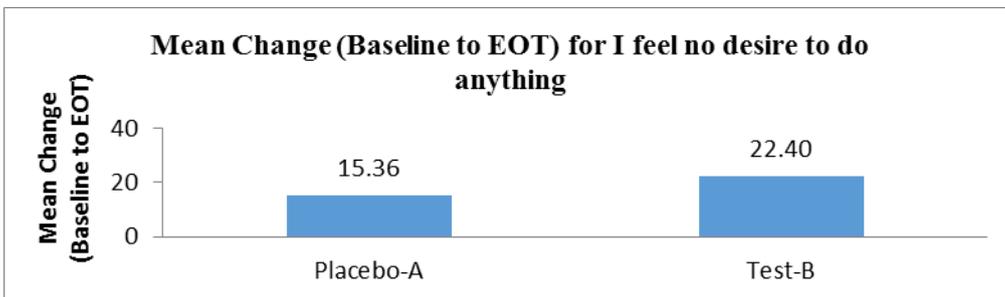


Fig. 8

Table 12		
Mentally, I feel exhausted		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	14.28	0.0002
Test-B	21.60	<.0001

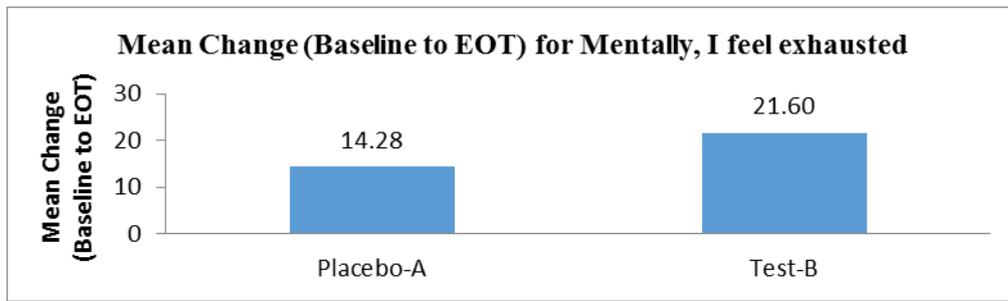


Fig. 9

**Table 13**  
When I am doing something, I can concentrate quite well

Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	13.80	0.0003
Test-B	20.00	<.0001

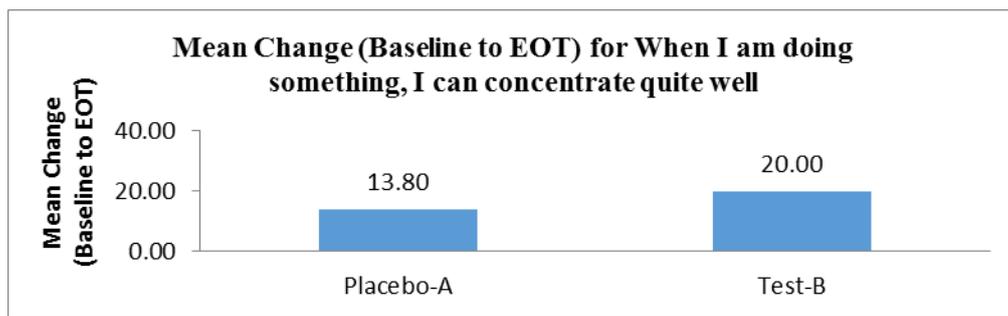


Fig. 10

**Table 14: Base Shift Change from Baseline to EOT for Fatigue assessment test.**

Drug Code	I am bothered by fatigue	I get tired very quickly	I don't do much during the day	I have enough energy for everyday life	Physically, I feel exhausted	I have problems to start things	I have problems to think clearly	I feel no desire to do anything	Mentally, I feel exhausted	When I am doing something, I can concentrate quite well
A	Improved	Improved	No Change	Improved	Improved	Improved	Improved	No Change	Improved	Improved
	Improved	Improved	No Change	Improved	Improved	Improved	Improved	Improved	Improved	Improved
	Improved	Improved	No Change	Improved	Improved	Improved	Improved	Improved	Improved	Improved
	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
	No Change	Improved	No Change	No Change	Improved	No Change	Improved	Improved	Improved	No Change
	No Change	Improved	Improved	Worsened	No Change	Improved	Improved	Improved	Improved	Improved
	No Change	No Change	Improved	No Change	No Change	No Change	Improved	Improved	Improved	No Change
	No Change	Improved	No Change	No Change	No Change	No Change	Improved	Improved	No Change	No Change
	Improved	Improved	No Change	No Change	No Change	No Change	No Change	No Change	No Change	No Change
	No Change	Improved	No Change	No Change	No Change	No Change	No Change	No Change	Worsened	No Change
	No Change	No Change	No Change	No Change	Improved	No Change	Improved	No Change	Improved	No Change
	No Change	No Change	No Change	No Change	No Change	No Change	Improved	Improved	Improved	Improved
	Improved	No Change	No Change	No Change	No Change	No Change	No Change	No Change	No Change	No Change
	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
	Improved	Improved	Improved	No Change	Improved	No Change	No Change	No Change	No Change	No Change
	Improved	Improved	Improved	Worsened	Improved	Improved	Improved	Improved	Improved	Improved
	Improved	No Change	No Change	No Change	Improved	Improved	Improved	Improved	Improved	No Change
	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	No Change	No Change
	B	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved		Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved		No Change	Improved	No Change	No Change	Improved	Improved	Improved	Improved	No Change
Improved		Improved	Improved	Improved	Improved	No Change	Improved	Improved	Improved	Improved
Improved		Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved		Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved		Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved		Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved		Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved		Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved

Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	No Change	Improved
No Change	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	No Change	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	No Change	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	No Change	No Change	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	Improved	No Change	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	No Change	Worsened	No Change	Improved	Improved	Improved	Improved	Improved	No Change
Worsened	Improved	No Change	No Change	Improved	No Change	No Change	Improved	Improved	Improved
Improved	Improved	No Change	Improved	Improved	Improved	Improved	Improved	No Change	No Change
Improved	Improved	No Change	Improved	Improved	Improved	No Change	Improved	Improved	Improved
Improved	No Change	Improved	No Change	Improved	Improved	Improved	No Change	Improved	Improved
Improved	Improved	No Change	Improved	Improved	Improved	Improved	Improved	Improved	Improved
Improved	No Change	No Change	No Change	Improved	Worsened	Improved	Improved	No Change	No Change
No Change	Improved	Improved	Improved	Improved	Worsened	No Change	Improved	Improved	No Change
Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved	Improved

**Table 15**  
**Table of Drug\_Code by I am bothered by fatigue**

Drug Code	I am bothered by fatigue			Total
	Improved	No Change	Worsened	
Placebo-A	18	7	0	25
Test-B	22	2	1	25
Total	40	9	1	50

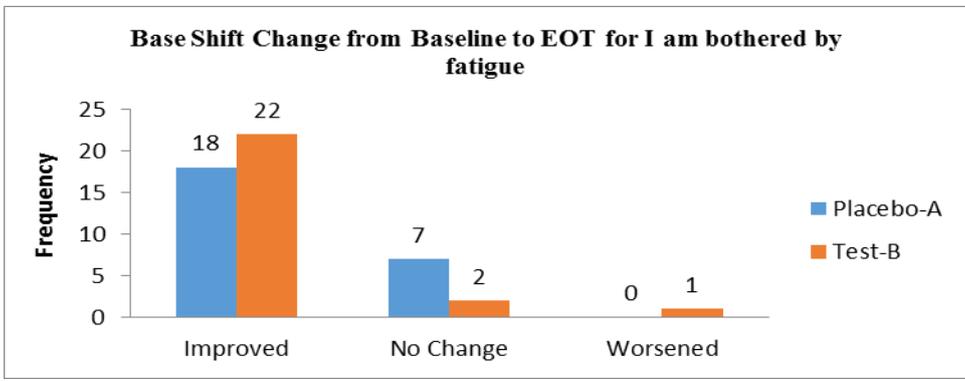


Fig. 11

**Table 16**  
**Table of Drug\_Code by I get tired very quickly**

Drug Code	I get tired very quickly		Total
	Improved	No Change	
A	18	7	25
B	21	4	25
Total	39	11	50

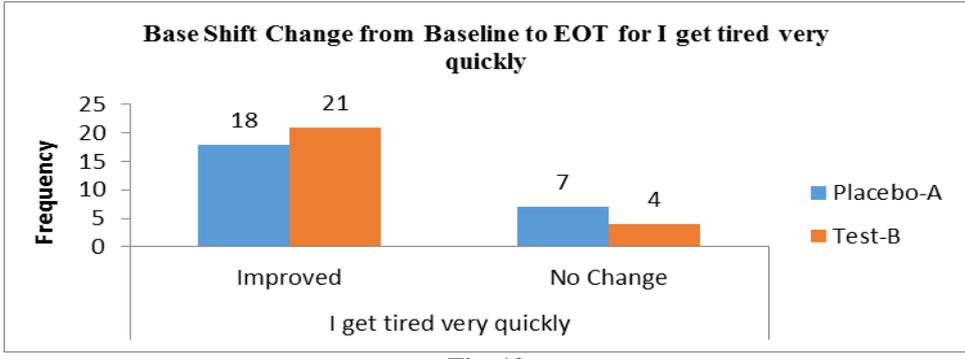


Fig. 12

Table 17				
Table of Drug_Code by I_don_t_do_much_during_the_day				
Drug Code	I don't do much during the day			Total
	Improved	No Change	Worsened	
Placebo-A	12	13	0	25
Test-B	15	9	1	25
Total	27	22	1	50

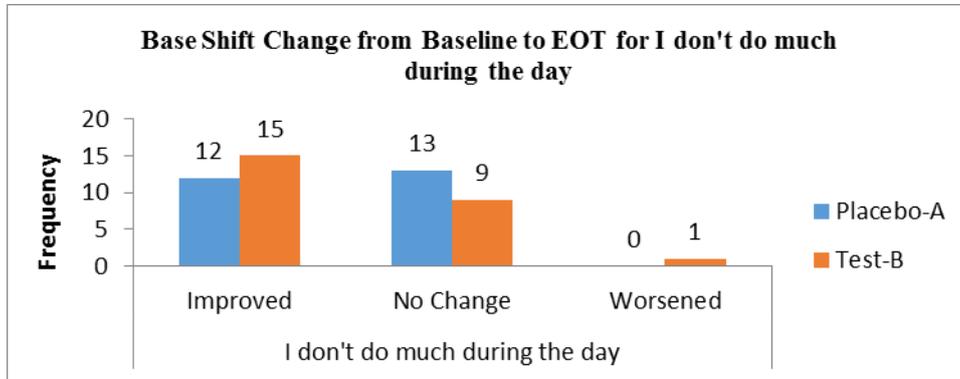


Fig. 13

Table 18				
Table of Drug_Code by I_have_enough_energy_for_everyday				
Drug Code	I have enough energy for everyday life			Total
	Improved	No Change	Worsened	
Placebo-A	11	11	3	25
Test-B	19	6	0	25
Total	30	17	3	50

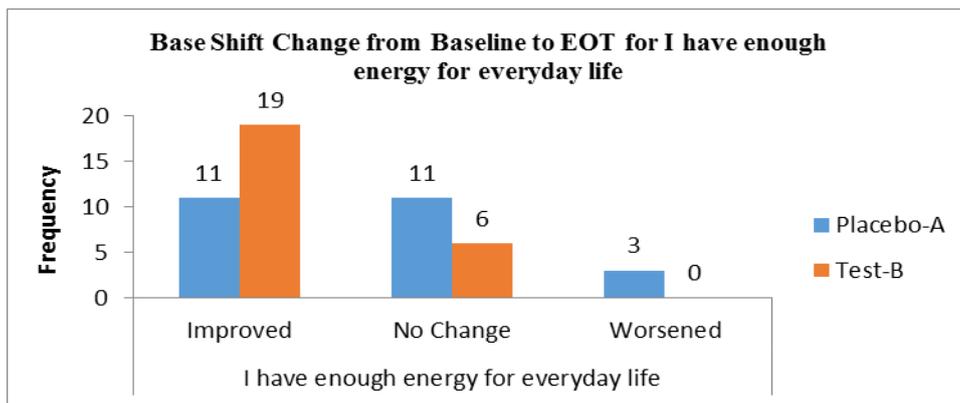


Fig. 14

Table 19			
Table of Drug_Code by Physically_I feel exhausted			
Drug Code	Physically, I feel exhausted		Total
	Improved	No Change	
Placebo-A	17	8	25
Test-B	23	2	25
Total	40	10	50

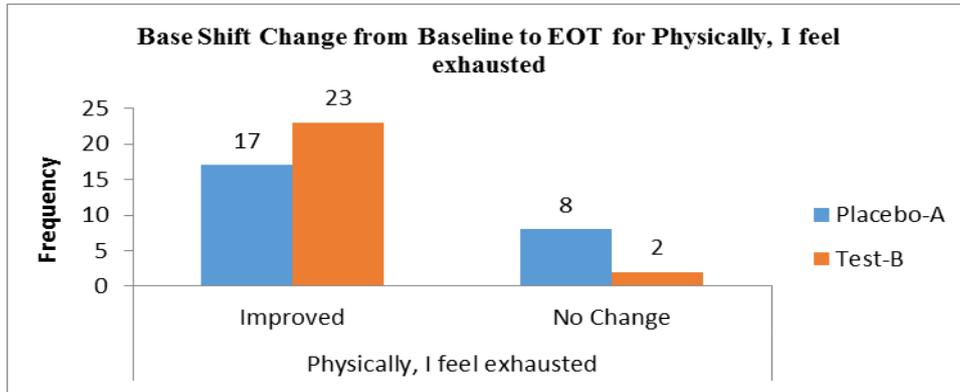


Fig. 15

Drug Code	I have problems to start things			Total
Frequency	Improved	No Change	Worsened	
Placebo-A	16	9	0	25
Test-B	20	2	3	25
Total	36	11	3	50

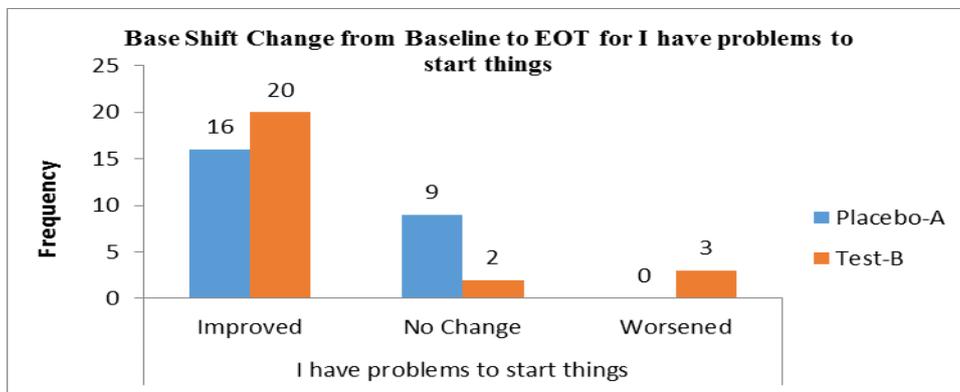


Fig. 16

Drug Code	I have problems to think clearly		Total
Frequency	Improved	No Change	
Placebo-A	21	4	25
Test-B	21	4	25
Total	42	8	50

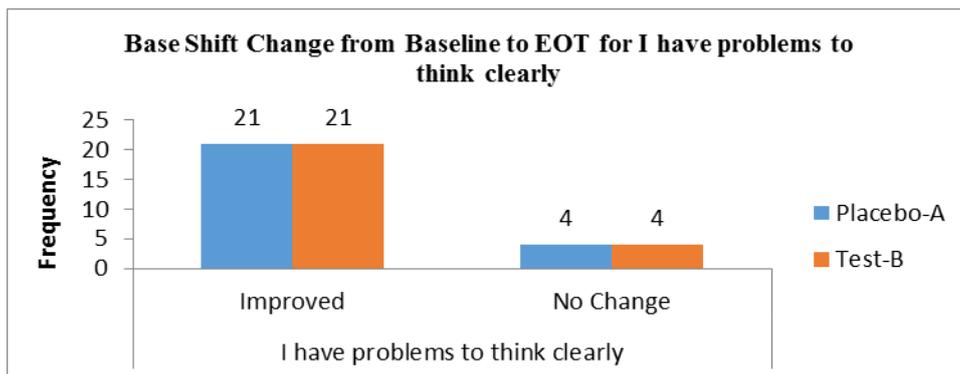


Fig. 17

**Table 22**  
**Table of Drug\_Code by I feel no desire to do anything**

Drug Code	I feel no desire to do anything			Total
	Improved	No Change	Worsened	
Placebo-A	18	6	1	25
Test-B	23	2	0	25
Total	41	8	1	50

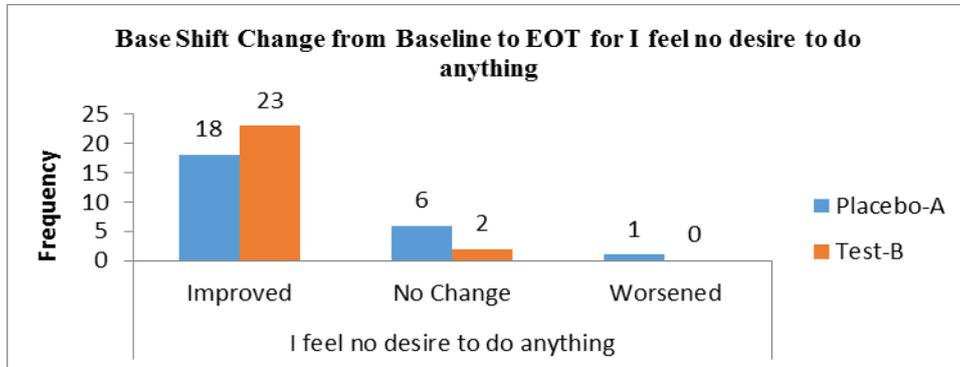


Fig. 18

**Table 23**  
**Table of Drug\_Code by Mentally, I feel exhausted**

Drug Code	Mentally, I feel exhausted		Total
	Improved	No Change	
Placebo-A	17	8	25
Test-B	22	3	25
Total	39	11	50

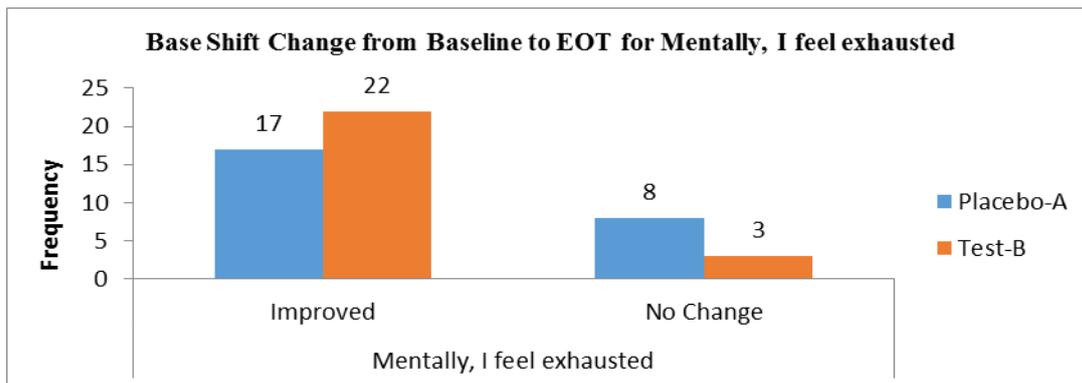


Fig. 19

**Table 24**  
**Table of Drug\_Code by When I am doing something I can**

Drug Code	When I am doing something, I can concentrate quite well		Total
	Improved	No Change	
Placebo-A	15	10	25
Test-B	19	6	25
Total	34	16	50

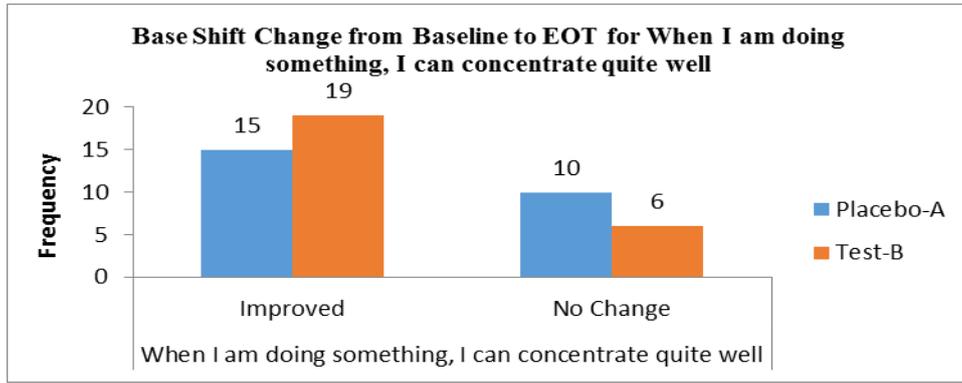


Fig. 20

2. Changes in severity of fatigue by using Fatigue Severity scale

**Table 25: T-test results for Total FSS Score.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	19.92	<.0001	14.64	25.20
Test-B	25.16	<.0001	20.32	30.01

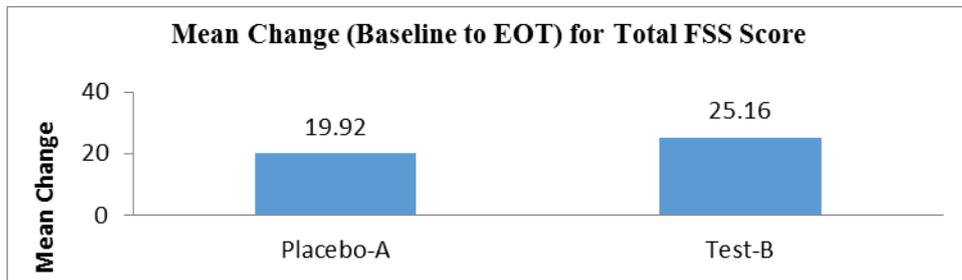


Fig. 21

**Table 26: T-test results for FSS Score.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	2.2133	<.0001	1.63	2.80
Test-B	2.7982	<.0001	2.26	3.34

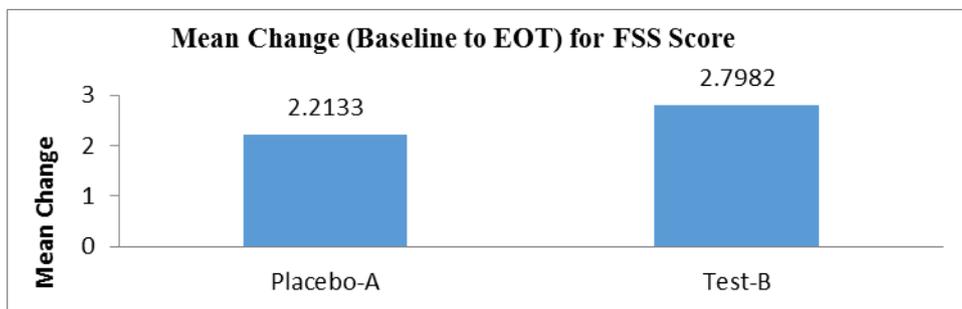


Fig. 22

Improvement in overall condition by assessing the Changes in Piper fatigue scale

**Table 27: Frequency distribution for feeling fatigue from Baseline to EOT for Placebo (A).**

Table of Visit_Name by How_long_have_you_been_feeling_					
Visit Name	How long have you been feeling fatigue?				Total
	Days	Months	Not feeling fatigue	Weeks	
SCR	0	11	0	14	25
Visit03	1	4	8	12	25
Total	1	15	8	26	50

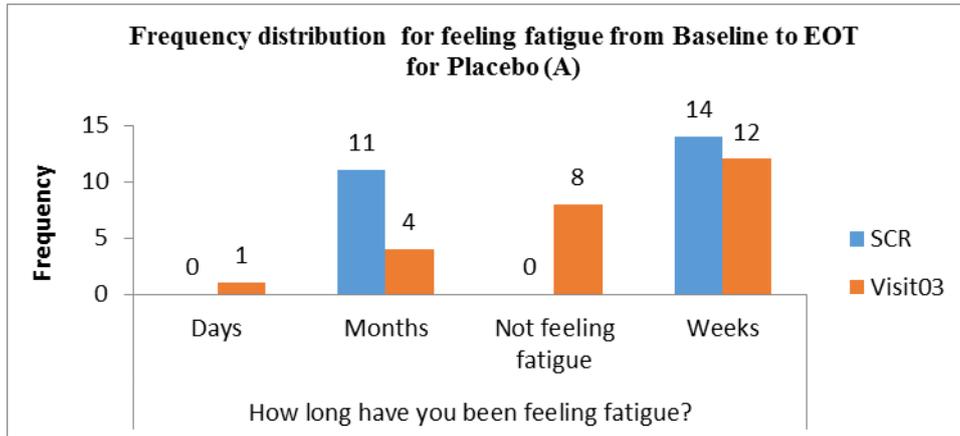


Fig. 23

**Table 28: Frequency distribution for feeling fatigue from Baseline to EOT for Test (B).**

Table of Visit_Name by How long have you been feeling f					
Visit Name	How long have you been feeling fatigue?				Total
Frequency	Days	Months	Not feeling fatigue	Weeks	
SCR	0	9	0	16	25
Visit03	1	3	12	9	25
Total	1	12	12	25	50

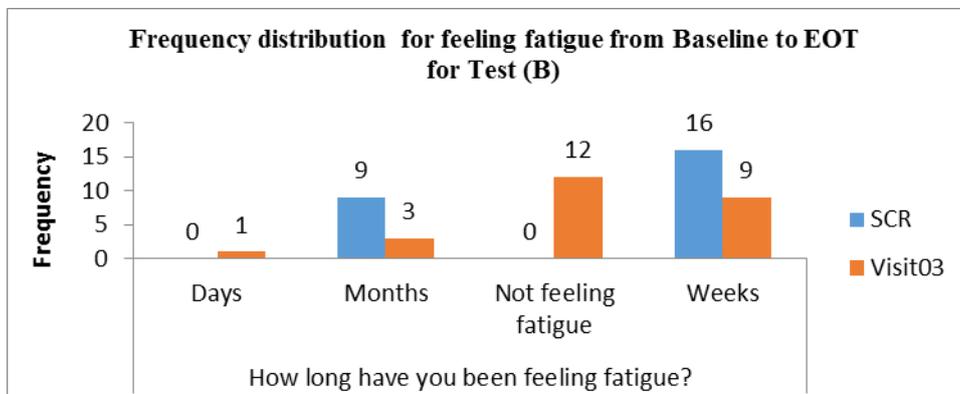


Fig. 24

**Table 29: T-test results for To what degree is the fatigue you are feeling now causing you distress from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	2.32	<.0001	1.31	3.33
Test-B	3.92	<.0001	2.91	4.93

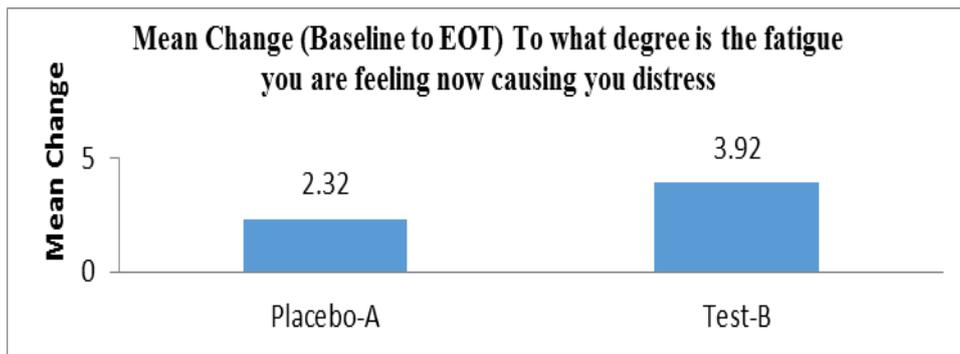


Fig. 25

**Table 30: T-test results for To what degree is the fatigue you are feeling now interfering with your ability to complete your work or school activities from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	3.00	<.0001	2.01	3.99
Test-B	3.96	<.0001	2.98	4.94

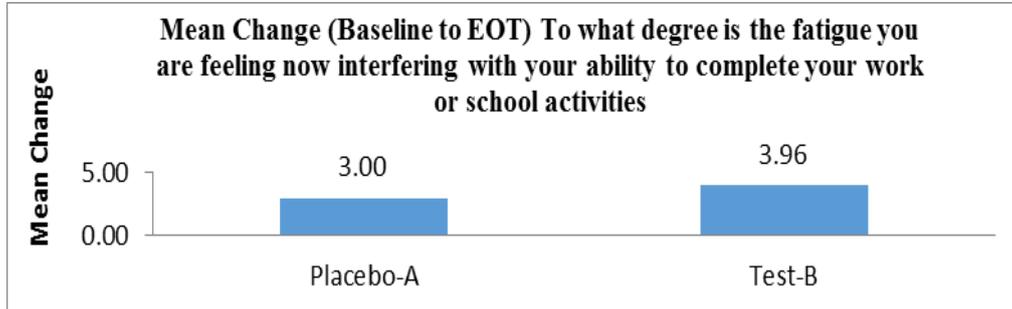


Fig. 26

**Table 31: T-test results for To what degree is the fatigue you are feeling now interfering with your ability to socialize from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	2.44	<.0001	1.47	3.41
Test-B	3.20	<.0001	2.09	4.31

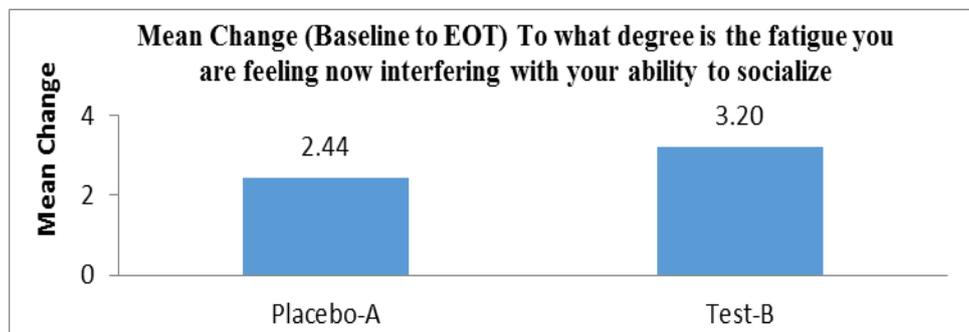


Fig. 27

**Table 32: T-test results for To what degree is the fatigue you are feeling now interfering with your ability to engage in sexual activity from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	0.84	<.0001	-0.50	2.18
Test-B	1.40	<.0001	0.22	2.58

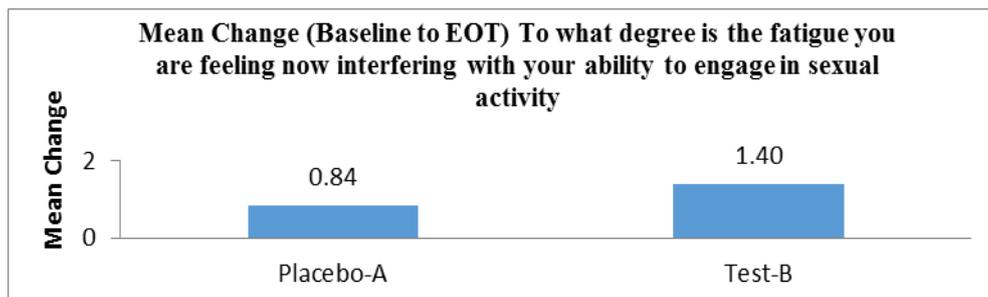


Fig. 28

**Table 33: T-test results for Overall, how much IS the fatigue which you are now experiencing interfering with your ability to engage in the kind of activities you enjoy doing from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	2.60	<.0001	1.68	3.52
Test-B	3.32	<.0001	2.37	4.27

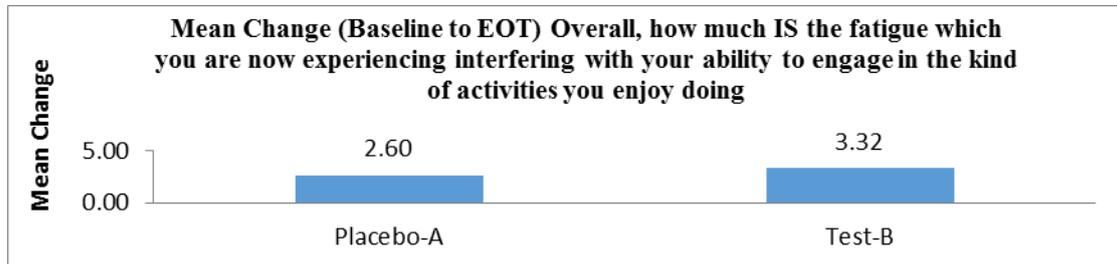


Fig. 29

**Table 34: T-test results for Overall, How would you describe the degree of intensity or severity of the fatigue which you are experiencing now from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	2.40	<.0001	1.52	3.28
Test-B	3.60	<.0001	2.60	4.60

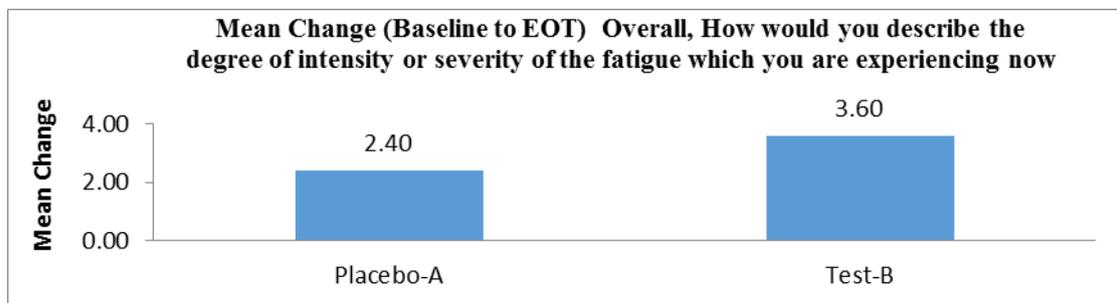


Fig. 30

**Table 35: T-test results for To what degree would you describe the fatigue which you are experiencing now as being from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	2.56	<.0001	1.73	3.39
Test-B	3.92	<.0001	2.89	4.95

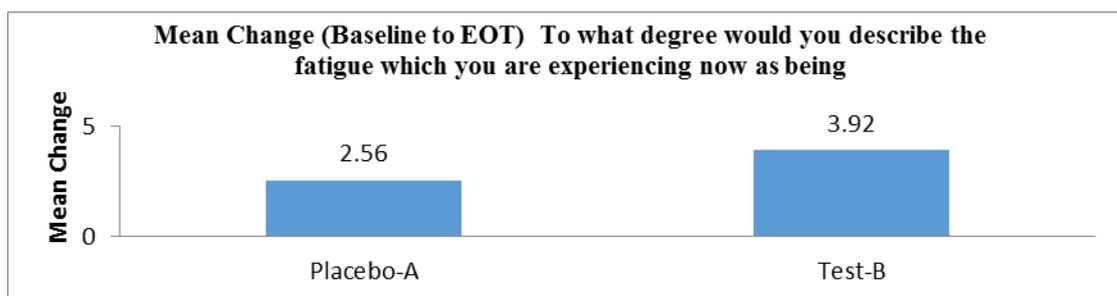


Fig. 31

**Table 36: T-test results for To what degree would you describe the fatigue which you are experiencing now as being from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	2.28	<.0001	1.08	3.48
Test-B	3.48	<.0001	2.38	4.58

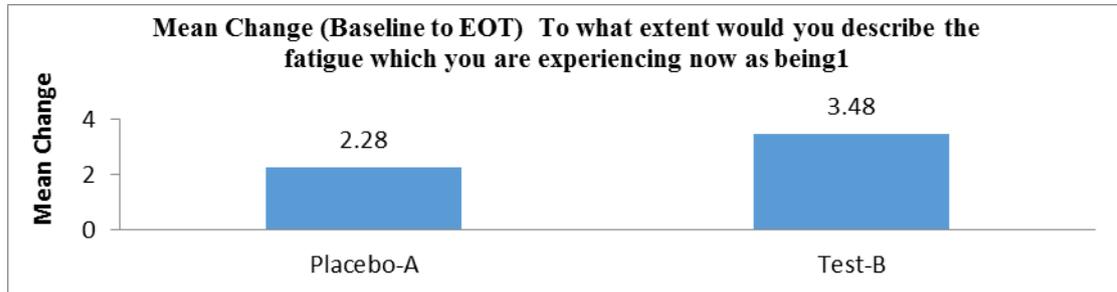


Fig. 32

**Secondary End-points**

Secondary endpoints consideration were Assessment of energy level by using Ergometer for instant energy and Changes in Chalder Fatigue Assessment scale.

**1. Assessment of energy level by using Ergometer for instant energy.**

Table 37		
Ergometer Scale (in min)		
Drug Code	Mean Change (Baseline to EOT)	p-value
Placebo-A	23.88	<.0001
Test-B	7.96	0.0225

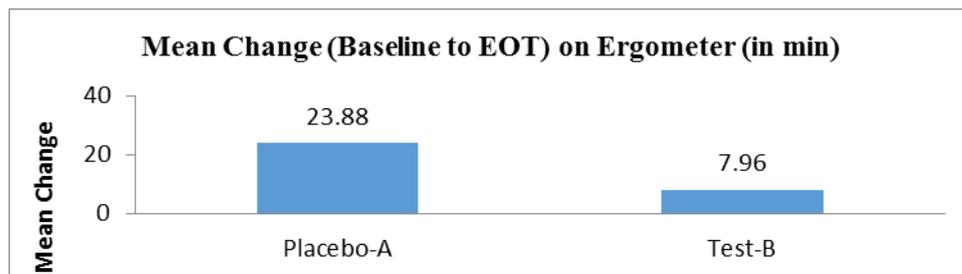


Fig. 33

**2. Changes in Chalder Fatigue Assessment scale**

Table 38: T-test results for Total Score as per Chalder fatigue Scale from Baseline to EOT.				
Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	10.20	<.0001	7.33	13.07
Test-B	13.32	<.0001	11.17	15.47

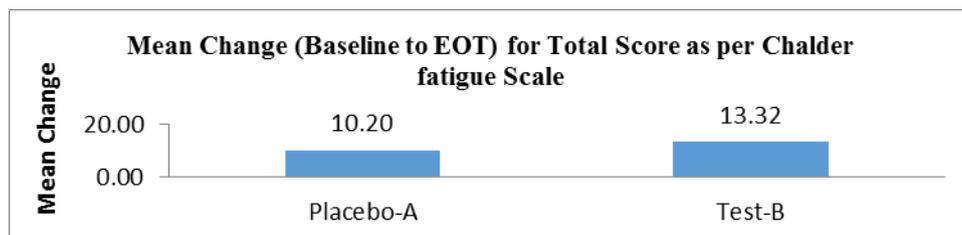
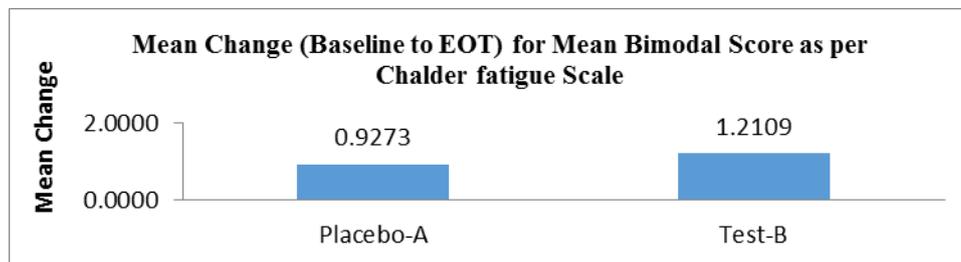


Fig. 34

**Table 39: T-test results for Mean Bimodal Score as per Chalder fatigue Scale from Baseline to EOT.**

Drug Code	Mean Change (Baseline to EOT)	p-value	95% Confidence Interval	
			Lower	Upper
Placebo-A	0.9273	<.0001	0.67	1.19
Test-B	1.2109	<.0001	1.02	1.41

**Fig. 35****14.0 Safety Evaluation****Adverse Events**

No serious and / or moderate adverse events were noted during the clinical trial, only 3 mild adverse events were

reported which lasted for less than 1 min, as mentioned below. So it is concluded that investigational product is safe to use.

**Table 40: Listing of Adverse events.**

Adverse Event Description	Is this a Serious Adverse Event (SAE)?	Intensity	Frequency	Study Medication Adjustment	Relationship to Study Medication	Outcome of Adverse Event
Dryness of mouth after taking IP	No	Mild	Isolated	None	Possible	Resolved with no sequelae
Dryness of mouth after taking IP	No	Mild	Isolated	None	Possible	Resolved with no sequelae
Dryness of mouth after taking IP	No	Mild	Isolated	None	Possible	Resolved with no sequelae

**DISCUSSION AND CONCLUSION**

Statistical Analysis of data obtained after the completion of study was analyzed using SAS<sup>®</sup> software for windows, version 9.1, at 5% level of significance ( $\alpha = 0.05$ ).

A total of 50 subject's data was obtained consisting of 25 subjects per treatment arms for Placebo-A and Test-B, respectively. Entire statistical analysis was performed as per the procedures mentioned in the study protocol. Descriptive statistics containing N (no. of observations), mean, standard deviation (SD), minimum and maximum were evaluated for all the continuous parameters.

Normality check of data was performed using Kolmogorov-Smirnov test statistic for Scores of Fatigue assessment test, Total FSS scores & FSS Scores of Fatigue Severity Scale at Baseline i.e., Screening and at EOT i.e., Visit 3. Among all the scores only Total FSS scores and FSS scores of Fatigue Severity Scale were found normal in nature at Baseline visit with p-values greater than 0.05, whereas rest of all other parameters i.e., Scores of Fatigue assessment test and Total FSS scores & FSS Scores of Fatigue Severity Scale at EOT were found to be non-normal in nature with p-values very much less than 0.05.

Separate analyses were performed for Placebo-A and Test-B, respectively. In which comparisons between screening and EOT values were made.

Wilcoxon Rank Sum Test was used to compare scores of various questions mentioned in fatigue assessment test to check for Improvement in fatigue level for Placebo-A and Test-B, respectively.

As per Table 4 for the question "*I am bothered by fatigue*" of Fatigue assessment scale, p-value was found to be <.0001 for both Placebo-A & Test-B products which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was 16.76 & 20.72 for Placebo-A & Test-B, respectively which indicates that Test-B is more effective in comparison to Placebo-A and the same is reflected in Fig. 1.

As per Table 5 for the question "*I get tired very quickly*" of Fatigue assessment scale, p-value was found to be <.0001 for both Placebo-A & Test-B products which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was 17.64 & 21.64 for Placebo-A & Test-B, respectively which indicates that Test-B is more effective

in comparison to Placebo-A and the same is reflected in Fig. 2.

As per Table 6 for the question “*I don't do much during the day*” of Fatigue assessment scale, p-value was found to be  $<.0001$  for Placebo-A and  $0.0002$  for Test-B product which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $12.24$  &  $13.80$  for Placebo-A & Test-B, respectively which indicates that Test-B is more effective in comparison to Placebo-A and the same is reflected in Fig. 3.

As per Table 7 for the question “*I have enough energy for everyday life*” of Fatigue assessment scale, p-value was found to be  $0.0165$  for Placebo-A and  $<.0001$  for Test-B product which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $8.56$  &  $17.60$  for Placebo-A & Test-B, respectively which indicates that Test-B is more effective in comparison to Placebo-A and the same is reflected in Fig. 4.

As per Table 8 for the question “*Physically, I feel exhausted*” of Fatigue assessment scale, p-value was found to be  $<.0001$  for both Placebo-A & Test-B products respectively, which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $16.88$  &  $21.00$  for Placebo-A & Test-B, respectively which indicates that Test-B is more effective in comparison to Placebo-A and the same is reflected in Fig. 5.

As per Table 9 for the question “*I have problems to start things*” of Fatigue assessment scale, p-value was found to be  $<.0001$  for both Placebo-A & Test-B products respectively, which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $17.24$  &  $19.60$  for Placebo-A & Test-B, respectively which indicates that Test-B is more effective in comparison to Placebo-A and the same is reflected in Fig. 6.

As per Table 10 for the question “*I have problems to think clearly*” of Fatigue assessment scale, p-value was found to be  $<.0001$  for both Placebo-A & Test-B products respectively, which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $20.32$  &  $20.40$  for Placebo-A & Test-B, respectively which indicates that Test-B & Placebo-A are having almost a similar change from Baseline to EOT values but still Test-B is more effective in comparison to Placebo-A and the same is reflected in Fig. 7.

As per Table 11 for the question “*I feel no desire to do anything*” of Fatigue assessment scale, p-value was found to be  $0.0002$  for Placebo-A &  $<.0001$  for Test-B product respectively, which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $15.36$  &  $22.40$  for Placebo-A & Test-B, respectively which indicates that Test-B is more effective than Placebo-A for change from Baseline to EOT values and the same is reflected in Fig. 8.

As per Table 12 for the question “*I feel no desire to do anything*” of Fatigue assessment scale, p-value was found to be  $0.0002$  for Placebo-A &  $<.0001$  for Test-B product, respectively which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $14.28$  &  $21.60$  for Placebo-A & Test-B, respectively which indicates that Test-B is more effective than Placebo-A for change from Baseline to EOT values and the same is reflected in Fig. 9.

As per Table 13 for the question “*When I am doing something, I can concentrate quite well*” of Fatigue assessment scale, p-value was found to be  $0.0003$  for Placebo-A &  $<.0001$  for Test-B product, respectively which shows that both Placebo-A & Test-B are showing significant statistical difference between Baseline and EOT values. Whereas, the mean change from Baseline to EOT was  $13.80$  &  $20.00$  for Placebo-A & Test-B, respectively which indicates that Test-B is more effective than Placebo-A for change from Baseline to EOT values and the same is reflected in Fig. 10.

Base shift Change from Baseline to EOT values was also calculated in order to assess the improvement in the fatigue levels of the patients for Placebo-A & Test-B separately which were categorized in three groups which reflects ‘Improved’, ‘No Change’ and ‘Worsened’ as mentioned in Table 14.

Further a frequency distribution was drawn for all the questions of Fatigue assessment test questionnaire. Results of the same are captured in Table nos. 15, 16, 17, 18, 19, 20, 21, 22, 23, & 24. All the tables and respective graphs are showing that Test-B is more efficacious in comparison to Placebo-A.

As per the results obtained from the Test of Normality for the Total FSS scores and FSS scores of Fatigue severity scale the scores were found normal in nature.

T-Test was used to compare the Total FSS scores from Baseline to EOT in Test-B and Placebo-A arm, separately. For Total FSS Score p-value was found to be  $<.0001$  for both Test-B and Placebo-A products. This shows that both Test-B & Placebo-A is showing statistically significant difference from Baseline to EOT

values. But as per Table 25 the mean change for Test-B & Placebo-A were 19.92 and 25.16, respectively which clearly indicates that Test-B is more efficacious than Placebo-A which is clearly reflected in Fig. 21.

T-Test was used to compare the FSS scores from Baseline to EOT in Test-B and Placebo-A arm, separately. For FSS Score p-value was found to be  $<.0001$  for both Test-B and Placebo-A products. This shows that both Test-B & Placebo-A is showing statistically significant difference from Baseline to EOT values. But as per Table 26 the mean change for Test-B & Placebo-A were 2.2133 and 2.7982, respectively which clearly indicates that Test-B is more efficacious than Placebo-A and the same is reflected in Fig. 22.

For assessing the improvement as per Piper Fatigue scale a frequency distribution showing change in fatigue severity from baseline to EOT was given for Test-B and Placebo-A arm, separately and it is clearly evident from Table 27, Table 28, Fig. 23 & Fig. 24 that Test-B is more effective in alleviating fatigue in comparison to Placebo-B.

Further T-test was used to assess the difference in scores of Piper fatigue scale questions and it was concluded from Table nos. 29, 30, 31, 32, 33, 34, 35, 36 and Fig. 25, 26, 27, 28, 29, 30, 31, 32 that Test-B is more efficacious in comparison to Placebo-A in alleviating fatigue.

Further an assessment was made on secondary end-points to measure the change in fatigue level from Baseline to EOT for Test-B and Placebo-A products separately.

Wilcoxon Rank sum Test was used for assessment of energy level for Ergometer readings from baseline to EOT values. This was done in order to measure the change from Baseline to EOT values for Test-B and Placebo-A product. For Placebo-A, p-value was obtained as  $<.0001$  whereas for Test-A p-value was calculated as 0.0225 which shows that both Test-B and Placebo-A product are showing statistically significant difference from Baseline to EOT values. But the mean change for Placebo-A and Test-B were evaluated as 23.88 & 7.96 which clearly shows that after receiving Test-B patients were able to work out for more time at EOT and this shows the efficacy of Test-B over Placebo-A.

T-Test was used to assess the difference in the Total and Bimodal scores of Chalder fatigue scale. As per Table 38, p-value for both Test-B and Placebo-A was found to be  $<.0001$  which shows that both Test-B and Placebo-A are showing statistically significant difference from Baseline to EOT values. But the mean change for Test-B is 13.32 whereas mean change for Placebo-A is 10.20, which clearly shows that Test-B is more efficacious in comparison to Placebo-A.

Considering the results and outcomes of all the primary and secondary end-points it is clearly evident that Instavit<sup>®</sup> instant energy oral spray is more efficacious than Placebo-A in alleviating the fatigue and improving alertness in day to day life.

## CONCLUSION

As per the study outcomes no serious and / or moderate adverse events were observed during the clinical trial, only 3 mild adverse events were reported which lasted for less than 1 min during the clinical trial and this concludes that investigational product is safe enough to use.

Also, the results obtained from Intra-group Statistical analyses and Efficacy analyses of Placebo-A and Test-B, as discussed above showed that Test-B was found to be effective in alleviating the fatigue and improving alertness in day to day life in comparison to Test-B.

So, this proves that Instavit<sup>®</sup> instant energy oral spray is more safe, efficient and superior in comparison to Placebo-A for implications on health and performance on everyday fatigue condition and improvement of alertness.

## REFERENCES

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