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Clinical Study Report

Protocol No: BNL-004

An Interventional / Prospective Phase III Accelerated Study To Determine The Efficacy & Safety Of RECEPTOL® Liquid Spray Used As A Stand-Alone Mono Therapy in HIV / AIDS Patients with multiple symptoms

1. TITLE PAGE

STUDY TITLE	An Interventional / Prospective Phase III Accelerated Study To Determine The Efficacy & Safety Of RECEPTOL® Oral Spray Used As A Stand-Alone Mono Therapy In HIV / AIDS Patients with multiple symptoms
PROTOCOL CODE	BNL-004
NAME OF INVESTIGATIONAL PRODUCT TESTED	RECEPTOL® Oral Spray
DEVELOPMENT PHASE OF STUDY	Phase III
INDICATION STUDIED	HIV/AIDS and related communicable diseases
TRIAL DESIGN	A STAND-ALONE, Interventional / Prospective, 12-week study in 50 subjects to determine efficacy & safety of treatment with RECEPTOL® on HIV viral load, Clinical & Physical Symptoms and Absolute CD4 cell counts in subjects with HIV / AIDS.
STUDY INITIATION DATE	October 15th, 2005
STUDY COMPLETION DATE	April 30th, 2006
SPONSORS	A2101 -04, Mansarovar, Neelkanth heights , Pokhran Rd 1, Thane West 400606, India What's all contact : +91 82910 84108
PARTICIPATING INSTITUTES	**PRINCIPAL INVESTIGATOR:** Dr. G.C. Rajadhyaksha, MD Medicine,

	Associate Professor: Dept. of Medicine, LTM Medical College and LTMG Hospital, Sion. Mumbai – 400 022, INDIA **STUDY CENTER:** Lokmanya Tilak Municipal Medical College & General Hospital Sion, Mumbai – 400 022, INDIA. Phone No: 2407 6381, Fax No: 2407 6100 **CENTRAL LABORATORY:** Metropolis Health Services Pvt. Ltd. Laboratory (NABL & CAP-USA accredited) Kasibhai Navrangi, Shri Niketan 8, Grant Road, Mumbai – 400 007, INDIA.

2. SYNOPSIS

NAME OF THE PRODUCT • RECEPTOL® ORAL SPRAY
NAME OF THE ACTIVE INGREDIENTS • RADHA 108 Series and Proline Rich Peptides (PRP)
TITLE OF THE STUDY • An Interventional / Prospective Phase III Accelerated Study To Determine The Efficacy & Safety Of RECEPTOL® Oral Spray Used As A Stand-Alone Mono Therapy In HIV / AIDS Patients with multiple Symptoms
STUDY SITE • Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai, INDIA
PUBLICATION(S) • None

TREATMENT PERIOD

• 3 Months

OBJECTIVES

Primary Objective
To evaluate the efficacy of RECEPTOL® liquid in HIV/AIDS patients in terms of reduction in HIV viral load and HIV/AIDS related clinical symptoms.

Secondary Objectives
To determine the effect of oral spray administration of RECEPTOL® liquid on:
• Change in Body Weight of patients
• Absolute CD4 cell count
• Overall Assessment of Efficacy and Safety/Tolerability of the RECEPTOL®.

METHODOLOGY

• This trial was a 12-week, Stand-Alone, study to evaluate the Efficacy and Safety/Tolerability of RECEPTOL® liquid in HIV/ AIDS patients.
• The potential subjects were screened after obtaining a written informed consent from (As per Schedule Y) the subject or LAR (Legally Acceptable Representative)/impartial witness.
• The study was designed to investigate efficacy of RECEPTOL® therapy in reducing Viral Load and clinical symptoms & increase in Absolute CD4 cell count & change in body weight.
• The study subjects received RECEPTOL® liquid as a spray self-administered by patients on either side of the oral buccal surface 6 times daily at every 4 hour's interval. Each administration consist a metered dose of 0.75 ml spray directly on the buccal mucosa.
• Subjects' body weight was monitored at every visit to determine the effect of RECEPTOL® therapy on change in the weight.
• The subjects were also assessed for clinical symptoms and physical findings which included HIV related Fatigue/Malaise, Diarrhoea, Nausea, Vomiting, Fever, Cough, Parasthesia Sleep Disturbance, Skin Rash, Herpes Zoster, Lymphadenopathy, Hair changes, oral thrush, Leukoplakia, Liver enlargement, Spleen enlargement, Weight of patient and Tuberculosis.
• Physician and Patient Overall Assessment scale were used to evaluate the efficacy and safety/ tolerability of RECEPTOL® liquid at the end of the treatment.

NUMBER OF PATIENTS

• A total of 50 patients completed the study.

INCLUSION CRITERIA

For recruitment in the study, the subjects were required to be :-

• Male and Female subjects between 18 and 60 years of age.
• Documentation of HIV infection by any approved ELISA test, and the disease contracted heterosexually (no drug abuse) preferably within six months of participation in this trial.
• With Absolute CD4 count greater than 100 cells/cmm
• With a measurable HIV viral load
• Subjects willing to give informed consent for their stay in the hospital and / or follow up visits.

EXCLUSION CRITERIA

Patients were not included in the study if they were :-

• Pregnant or nursing women, women of childbearing potential not using an adequate method of birth control.
• Subjects with kidney failure with Serum Creatinine greater than 1.5 mg/dL.
• With a history of Hepatic Cirrhosis.
• Suffering from Congestive Heart Failure (CHF).
• With current alcohol or substance abuse that could interfere with patient compliance.
• Organ transplant recipient.
• With Preexisting Uncontrolled Seizure Disorder.
• Using long term systemic corticosteroids, Immuno-suppressive and ART.

CRITERIA FOR EVALUATION

Safety

• Safety assessments consisted of monitoring and recording all Adverse Events including Serious Adverse Events.

Efficacy

• The primary efficacy variable was a statistically significant reduction in HIV viral load based

on PCR measurement and HIV related clinical symptoms and physical findings via symptom assessment form.

• The secondary efficacy variables were change in body weight and an increase in Absolute CD4 cell count based on Flow Cytometry Analysis of blood.

• An Overall Assessment of Efficacy and Safety/Tolerability was made by both, the treating Physician and the participating patients.

STATISTICAL METHODS

• Case Report Forms completed in all respects and reports from the Principal Investigator were evaluated at the **Department of Biostatistics, All India Institute of Medical Sciences**, New Delhi. The primary efficacy end point was the effect of therapy on the markers of HIV disease including HIV viral load and HIV related clinical symptoms while the secondary efficacy end points were body weight gain & increase in Absolute CD4 cell count along with the general well being of the patients. The data on Absolute CD4 counts and HIV viral load was taken from the CRFs provided at baseline and at Week 11 (End of Treatment) while body weight of the subjects was monitored every week. Clinical symptoms and physical findings ware analyzed by using chi-square test at 5% level of significance. Whereas the body weight gain was calculated using paired sample t-test at 5% level of significance.

• The change in median HIV viral load and Absolute CD4 cell count was statistically calculated from Baseline to Week-12 using Wilcoxon signed Rank test at 5% level of significance.

• Overall Assessment of Efficacy and Safety/Tolerability recorded at the end of treatment by Physicians and Patients was calculated by using frequency distribution and percentage.

STUDY RESULTS

Efficacy Results

• **HIV viral load based on PCR Diagnosis**: At the end of 12-Weeks Treatment (end of the study) with RECEPTOL®, median value of Viral Load showed a significant change ($p<0.001$) calculated by Wilcoxon signed Rank test from baseline as evident in the statistical analysis. These measurements were made at independent NABL Accredited Central Metropolis Laboratory in Mumbai at the beginning (baseline) and at the end of the 11 weeks trial.

• **Improvement in Clinical Symptoms & Physical Findings**: There was a marked improvement

in HIV related clinical symptoms and many patients became asymptomatic at the end of 3 Weeks therapy ($p < 0.05$). At baseline, 88% of Patients had Fatigue/Malaise which became asymptomatic after 6th week of treatment with RECEPTOL®. HIV related Diarrhoea was cured in all patients from 5th Week onwards with significant fall from 3rd Week, Nausea disappeared from 5th Week onwards with significant fall from 3rd Week onwards. HIV related Vomiting had significant fall after 4th Week and all patients became asymptomatic after 7th Week onwards**.** Significant fall in Fever and related symptoms was observed in all HIV patients after 4th week and became asymptomatic after 7th week onwards. HIV related Cough had a significant fall from 3rd week onwards and all patients became asymptomatic from 10th week onwards. HIV related Tuberculosis patients became asymptomatic from 2nd week onwards. HIV related Disturbed Sleep patients had a significant improvement after 2 weeks of treatment and became asymptomatic after 5th week. HIV related Skin Rash had a significant fall at the end of 2nd week and all patients reported no rashes from 4th week onwards. HIV related Herpes Zoster had a significant fall at the end of 3rd week and became asymptomatic in all patients after 4th week with the treatment RECEPTOL®.

• **Absolute CD4 Cell Count**: At the end of 12-Weeks Treatment (end of the study) with RECEPTOL®, median value of Absolute CD4 counts compared to baseline the p=0.06 based on Flow Cytometry Analysis conducted at Central Metropolis Laboratory in Mumbai.

• **Weight Gain (Monitored Weekly)**: A significant increase was evident in bodyweight of all the 50 HIV positive patients who completed the trial treatment. A mean gain of 4.73 kg in body weight ($p<0.05$) was seen at the end of 11 weeks trial treatment with RECEPTOL®. The gain in body weight ranged between 3 to 7 kgs.

Safety & Tolerability Results

• **All patients tolerated** RECEPTOL® well with No Adverse or Serious Adverse Events.

Overall Efficacy & Safety/Tolerability Assessment by Investigator & Patient

• **According to Investigators Assessment**: 90.57% of the patients showed Very Good, Good or Satisfactory results for efficacy of the trial drug treatment.

• **According to Investigators Assessment** : 94.34% of the patients showed either Very Good orGood results in terms of the safety/tolerability of the trial drug treatment

• **According to Patients Assessment:** 92.46% of the patients showed either Very Good, Good or Satisfactory results for efficacy of the trial drug treatment.

• **According to Patients Assessment:** 79.25% of the patients showed Very Good and Good results for the safety/ tolerability of the trial drug treatment while 15.09% of the patients experienced no side effects.

CONCLUSION

• Treatment with RECEPTOL® had a clinically relevant and consistent effect in patients with HIV/AIDS disease. The HIV viral load assessed by PCR method showed a significant reduction from the baseline values. The Absolute CD4 counts showed a significant increase from baseline, at the end of 11 weeks therapy with RECEPTOL® as analyzed by Flow Cytometry method. The Clinical & Physical HIV related symptoms improved drastically with the therapy and most of the patients became asymptomatic within 3 weeks after the start of RECEPTOL®. The 11 weeks trial treatment with RECEPTOL® was well tolerated with no incidence of any side effects/Contraindication reported in any of the patients studied. The results showed that RECEPTOL® is an effective and safe natural product/drug in increasing weight and general well being of patients, decrease in HIV viral load and increase in Absolute CD4 cell count. Thus RECEPTOL® is a new, safe and natural therapeutic option for HIV / AIDS and other immuno-compromised patients. It can also work as an immunomodulator and can boost the immunity as an adjunct therapy for life-threatening critical ailments and recurrent infections from communicable diseases.

3. STATEMENT OF COMPLIANCE

This study was conducted in compliance with the Protocol as well as the Sponsor's and CRC's (CRO) **Standard Operating Procedures**. These were designed to ensure adherence with the ethical principles that have their origin in the **Declaration of Helsinki, Good Clinical Practice (GCP)** and applicable regulatory requirements. Also in accordance with **'Guidelines for Clinical Trials on Pharmaceutical Products in India-GCP Guidelines'** issued by the Central Drugs Standard Control Organization (CDSCO), Ministry of Health, Government of India.

4. LIST OF ABBREVIATIONS AND DEFINITIONS

List of Abbreviations

- **AIDS** Acquired Immunodeficiency Syndrome
- **ART** Anti-Retroviral Therapy
- **ARS** AIDS Related Complex
- **CD4** Cluster Of Differentiation 4
- **CD8** Cluster Of Differentiation 8
- **CHF** Congestive Heart Failure
- **CRC** Clinical Research Coordinator

- **CRF** Case Report Form
- **CRO** Contract Research Organization
- **CDSCO** Central Drugs Standard Control Organization
- **cmm** Cubic Millimeter
- **DCGI** Drug Controller General of India
- **DGHS** Director General Health Services
- **dL** Deciliter
- **ELISA** Enzyme Linked Immuno Sorbent Assay
- **GCP** Good Clinical Practice
- **Hb** Haemoglobin
- **HIV** Human Immunodeficiency Virus
- **ICMR** Indian Council Of Medical Research
- **IIH** Institute of Immuno-Heamatology
- **INF** Interferon
- **mm3** Per cubic millimetre
- **ml** Millilitre
- **mg** Milligram
- **NABL** National Accreditation Board for Testing and Calibration Laboratories
- **NACO** National AIDS Control Organization
- **NKC** Natural Killer Cell
- **NNRTI** Non-Nucleoside Reverse Transcriptase Inhibitor

- **NRTI** Nucleoside Reverse Transcriptase Inhibitor
- **PCR** Polymerase Chain Reaction
- **PRP** Proline-Rich Polypeptide
- **SGOT** Serum Glutamic Pyruvic Transaminase
- **SGPT** Serum Glutamic Oxaloacetic Transaminase
- **TNF** Tumor Necrosis Factor
- **WBC** White Blood Corpuscle
- **WHO** World Health Organization

Definitions of Terms

- **Eligible:** Qualified for enrolment into the study based on strict adherence to inclusion and exclusion criteria.
- **Evaluable:** Meeting all eligibility criteria, complying with the procedures defined in the Protocol and therefore included in analysis.
- **Investigator:** Treating physician.
- **Subject(s):** Term used throughout this report to denote the enrolled individual(s).

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6. ETHICS COMMITTEE

This study was conducted in accordance with the ethical principles of Declaration of Helsinki. Ethical approval of the Study Protocol was obtained from the Ethics Committee at Institution (Lokmanya Tilak Municipal Medical College & General Hospital, Sion, Mumbai) where the study was conducted before the study was undertaken. The approval of the Ethics Committee was given in writing on **February 24, 2005.** The original documents were sent to Sponsor and the Investigator filed a copy. In addition, all local regulatory requirements were adhered to. All attempts were made to protect the interest of the study patients.

The Institution review broad consisting of scientific and ethics committee's under the research society of LTMMC and LTMG Sion hospital, Mumbai has approved the following: Study Protocol/Amendment(s), written Informed Consent Form including patient information sheet, consent form updates and patient recruitment procedures. The EC notifications were followed as per Good Clinical Practice Guidelines issued by Central Drugs Standard Control Organization (CDSCO) and Ethical Guidelines for Biomedical Research on Human Subjects issued by Indian Council of Medical Research (ICMR).

7. INVESTIGATORS AND STUDY ADMINISTRATIVE STRUCTURE

Investigators:

PRINCIPAL INVESTIGATOR

Dr. G.C. Rajadhyaksha, MD Associate Professor: Dept. of Medicine, LTM Medical College & Sion Hospital, Mumbai 400 022, INDIA

CO-INVESTIGATORS

• Dr. Neelam Redkar, Associate Professor: Dept. of Medicine, LTM Medical College & Sion Hospital, Mumbai 400 022, INDIA

• Dr. Rupal Malye, Assistant Professor: Dept. of Medicine, LTM Medical College & Sion Hospital, Mumbai 400 022, INDIA

Project Coordinator:

Dr. Pawan Saharan*, Chairman & CEO Biomix Network Ltd., Millennium Business Park, Unit No.303, Building 6, Sector-3, M. I. D. C., Mahape, Navi Mumbai, Maharashtra - 400 709, INDIA

*Based on January 12, 2005 notification of Ministry of Health, Government of India.

Study Centre:

Lokmanya Tilak Municipal Medical College & General Hospital Sion, Mumbai 400 022, INDIA

Sponsor:

Ministry of Health; National AIDS Control Organisation (NACO), Government of India and Biomix Network Limited Millennium Business Park, Unit No.303, Building 6, Sector-3, M. I. D. C., Mahape, Navi Mumbai, Maharashtra - 400 709, INDIA

Central Laboratory:

Metropolis Health Services Pvt. Ltd. Laboratory (NABL & CAP-US accredited) Kasibhai Navrangi, Shri Niketan 8 Near Gamdevi Police Station, Grant Road, Mumbai – 400 007, Maharashtra, INDIA

Trial Statistician:

Dr. Guresh Kumar (Scientist), M.Sc., M.Phil., PhD (Statistics): Dept of Biostatistics, All India Institute of Medical Sciences, Ansari Nagar, New Delhi – 110 029, INDIA

Monitored By:

• Dr. Ganga Khedkar, Dy Director National AIDS Research Institute (NARI), Plot No. 73, Block G, MIDC Complex, Bhosari, Pune – 411026, INDIA

• Dr. Urmila Thatte, HOD Dept of Clinical Pharmacology, Nair Hospital, C Buddha Vihar Marg Kamathipura, Mumbai, INDIA

8 INTRODUCTION

Introduction: HIV/AIDS and Types of Treatment:

The advent of HIV/ AIDS has graphically demonstrated that our knowledge of viruses and how to treat viral infections was not adequate. According to the joint United Nations program on HIV/AIDS and World Health Organization (WHO), some 25 million people have died of HIV/AIDS in the past 25 years and an estimated 38.6 million are infected with the virus, making it one of the most lethal epidemic in the history of mankind. Currently five classes of drugs are approved by US FDA for treatment of HIV infected patients. These five classes are Nucleoside Reverse Transcriptase Inhibitor (NRTI/NtRTI), Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI), Protease Inhibitor (PI), entry inhibitors and Integrase Inhibitor. Anti Retroviral Therapy (ART) regimen is complicated due to the high cost of treatment, poor compliance, pill burden, peculiar storage requirements, drug-drug interactions, comorbidities like tuberculosis, liver disease, cardiovascular complications and importantly treatment failure due to resistance to drugs acquired by the virus through mutation. All the antiviral drugs developed so far to fight HIV infection, exhibit serious side effects like Nausea, Diarrhoea, Vomiting, Pancreatitis,

Anaemia, Peripheral Neuropathy, Lactic Acidosis, Dyslipidemia and others. Currently, the US FDA has approved 29 drugs for use in the treatment of HIV Infection5. The presently available ART is very expensive. The future outlook for HIV / AIDS treatment from a pharmaceutical perspective remains bleak despite significant gains in understanding of the virus. This situation has forced scientists to look for alternative effective solutions.

A promising alternative which may prove more effective can be to stimulate the body's own defenses against the virus as well as the infected cells. Dietary supplementations of many naturally occurring substances have been claiming to boost human immunity by activating human Natural Killer (NK) cell activity. One such area of investigation is based on an age-old remedy, the Colostrum, the first milk produced by a mammal following the birth of a newborn, which was widely used as an immunity booster and natural antibiotic before modern antibiotics were developed. Colostrum and various components of it have already been demonstrated to be useful in treating opportunistic infections related with HIV/ AIDS. such as Diarrhea etc. caused by Clostridium, Campylobacter and Amoeba spc.13. Specifically one of the components of Colostrums, the nano-peptides classified under Radha 108 series (Patent pending by Biomix Network Ltd.) and Proline Rich Polypeptide (PRP) – Infopeptide has shown great promise. This unique polypeptide (a peptide fraction of whole Colostrum) has been shown to exhibit Immunomodulatory activity as well as antiviral activity14. The advantage of these compounds over conventional antiretroviral drugs is that these display a much shorter response time for alleviation of physical and clinical symptoms of the disease and a relatively quick normalization of NK activity. It is the only Immunomodulator produced by mammals themselves for their progeny. The key factor is however, the protein fractionation and ultra filtration technology needed to extract Radha 108 and Proline-Rich Polypeptide (PRP) extraction which is developed now by Biomix Network Ltd using patented technology and molecular weight exclusion columns to ensure consistency of product batch after batch in every bottle of RECEPTOL®.

RECEPTOL®: Product Development Rationale

The application of RECEPTOLTM is, in the medical field of Immuno-therapy which is a quiet revolution taking place in medicine. It is a form of treatment that uses the different aspects of your immune system, its cells and molecules and its various stratagems to tip the balance in your favor as your body battles to maintain health. RECEPTOL® comes to us after nearly fifty years of research and over 3,500 scientific medical papers, which prove its effectiveness. It is found in colostrum and is a natural way of strengthening our immune systems against disease.

RECEPTOL® contains the Nano-Informational Peptides (RADHA108) and Proline-Rich Polypeptides (PRPs), derived from bovine Colostrum, which helps in strengthening the body'sown immune system against diseases in a natural way.

The Nano-polypeptides have been known for long for their antiviral, anti-inflammatory and immune enhancing properties. However, the molecular mechanism of their action in conjunction with low molecular weight Nano-peptides was not known until *Dr. Theodore Damodar Singh*, an Applied Biochemist from University of California Irvine and Founder Director, Chaitanya Healthcare, India and Dr. Pawan Saharan, Chief Scientific Officer and Founder Director, Chaitanya Healthcare and Biomix Network Ltd., India identified and studied a series of *Nano-Informational Peptides (RADHA1081-100)* from Bovine Colostrum. The fusion of viral particles with human white blood cells occurs with the aid of glycoprotein epitopes on the viral wall. The informational proteins (RADHA1081-100) in RECEPTOL® have been shown to mitigate cell fusion. The RADHA1081-100 series of molecules may dock on the glycoprotein receptors of the viral surface mimicking their receptors on the cell surfaces and thus block the virus entry into the immune cells. One of the Immunomodulator action of RECEPTOL® is to stimulate the maturation of immature thymocytes into either helper or suppressor T cells4,5, depending on the need of the body at a given time. Helper T cells present antigens (such as viral protein) to B lymphocytes, which in turn produce antibodies to that antigen6. Helper T cells also help produce memory T cells which retain the memory of an antigen in order to expedite the production of antibodies in the event the antigen is reencountered in the future7. Suppressor T cells, on the other hand, have been shown to deactivate other lymphocytes after an infection has been cleared to avoid damage to healthy tissues8. RECEPTOL® may also promote growth and differentiation of B-cells in response to an infection9 and the differentiation and maturation of macrophages and monocytes10. The activity of Natural Killer (NK) cells, cytotoxic cells of the innate immune system, is increased by up to 5-fold by RECEPTOL®11, 12.

RECEPTOL® may modulate the cytokine system as well. Its constituents have been shown to stimulates the production of a wide range of cytokines, including the pro-inflammatory cytokines Tumor Necrosis Factor – Alpha (TNF-_) and Interferon Gamma (INF–_) and anti-inflammatory cytokines Interleukin – 6 and – 1013. The constituents of RECEPTOL® may function as a molecular signaling device which works through receptors on target cell surfaces14 to initiate or suppress the production of specific proteins. This property is not species specific2; and hence the constituents of RECEPTOL® derived from bovine Colostrum may work as effectively in humans too like the PRP of human Colostrum. There are no known side effects or drug interactions with the constituents of Colostrum, and it may be taken safely by patients of all ages. In an experimental in vitro system, the constituents of RECEPTOL® have been shown to

effectively block HIV infection of cells15. RECEPTOL® in combination with Zidovudine®, a known anti-retroviral drug, has been shown to be effective in patients suffering from HIV/AIDS Related Complex (ARC), affecting an increase in White Blood Cells, CD8 lymphocytes and IL-216. RECEPTOL® has shown to be effective in treating many different diseases and conditions including Allergies, Thrush, Diabetes (type II), Rheumatoid Arthritis, Corneal Regeneration, Diarrhoea, Hemolytic Anemia, Tuberculosis, HIV, Hepatitis A & C, Acute Viral Infections, Pharangitis (Viral), Viral Respiratory Infection, Plantar Warts, Colds and Flues, Herpes Simplex I & II etc.

Results of Previous Phase I, II & III International Studies

RECEPTOL® demonstrated in-field and clinical use with more than 10,000 HIV infants, children and adults in many countries. There have been no known exceptions to the ability to affect the progression of many chronic degenerative diseases for which it has been used. In many cases, the formula has induced what appears to be complete and lasting cellular recovery. RECEPTOL® has shown to be effective in treating many different diseases and condition. However, it is prudent to focus attention on a few well-known diseases. Initially, Rheumatoid Arthritis was the selected disease to put under the microscope. The success of treating this autoimmune condition led to the selection of a high profile disease – HIV. RECEPTOL® has been used with positive results in more than 10,000 patients globally for HIV & other Viral infections, Tuberculosis, immunological diseases. *RECEPTOL® Phase I trial in Ohio, USA:* This trial was conducted on 12 HIV patients with 30 days treatment of moderate control of product use. Results obtained from this trial were 10 out of 12 patients gained weight during the thirty-day trial period, of the 10 that gained weight, 7 (70%) gained an average of 6 lbs, 5 patients gained 6 lbs in one month, while 2 others 5.5 and 6.6 lbs respectively, the highest weight gain of 12 lbs was recorded for a patient who had been HIV positive since 1986 (10 years). 8 out of 10 patients had various levels of diarrhoea (mild, moderate or severe) at the beginning of the trial period. Out of the 8, 5 patients (62%) went from varying levels of diarrhoea severity to No diarrhoea symptoms. The 1 patient without weight gain experienced total elimination of severe chronic diarrhoea and a return to solid stool formation. 8 out of 12 patients had various levels of nausea at the beginning of the trial period. Of the 8, 5 patients (62%) went from varying levels of severity of nausea symptoms to No nausea. Of the remaining 3 patients, with some degree of nausea, 2 experienced a reduction in the severity of their symptoms. 9 out of 10 patients, who reported fatigue symptoms at the beginning of the trial, experienced an increase in their level of energy. 3 out of 10 experienced a significant increase in energy, from initial varying levels of fatigue to No fatigue. 4 out of 12 had either a mild to moderate cough at the beginning of the trial. 2 of the 4 reported No cough at the end of the trail period. Of the remaining 2 individuals, 1

reported a reduction in the severity of his cough. All 12 patients experienced an improvement in their overall symptoms assessment score. The average reduction approached 2/3 (63%) – Dr Brandt. Since 1996, several improvements in the process engineering were made to increase the efficacy of RECEPTOL®.

RECEPTOL® Phase II trial in Nairobi, Kenya (August 2000): This trial was conducted in 30 HIV patients with 90 days treatment of moderate control of product use. The objectives of this study were to demonstrate, under clinical conditions, the Efficacy and Safety of Infoprotein supplementation in patients known to have advanced disease (HIV/AIDS), compromised immune resources and limited access to conventional treatment. Positive clinical results were observed in the Nairobi patients. The results demonstrated that the product appeared to be free of side effects and generally well tolerated by the participants. Some signs, consistent with detoxification, were noted but resolved when the patients increased their water consumption. The product demonstrated significant value by reducing or resolving the symptoms of opportunistic infections most commonly related with the dynamic of HIV/AIDS. Patients often experienced weight gains as part of an overall pattern of positive response.

Conclusion: Because of differences in size, cohort profile and length of evaluation period, the Nairobi study yielded a greater quantity of information that included positive clinical responses in three additional areas: hypertension, systemic lupus and tuberculosis. Several patients that had been bedridden for some time became ambulatory and were able to come to the clinic for continued participation in the study.

RECEPTOL® Phase III trial Rwanda, Africa (November 2002): This trial was conducted in 60 HIV patients with 365 days treatment of moderate control of product use. The objectives of this study were to demonstrate, under clinical conditions, the Efficacy and Safety of Infoprotein supplementation in patients known to have advanced disease (HIV/AIDS). Cohorts were all symptomatic, ambulatory, compliant and native to Anti-Retroviral Therapy. All patients received RECEPTOL® every 6 hours for a period of 365 days. Positive clinical results were continually observed in the Rwanda patients. The results demonstrated that the product appeared to be free of side effects and generally well tolerated by the participants. Some signs, consistent with detoxification, were noted but resolved when the patients increased their water consumption. The product demonstrated significant value by reducing or resolving the symptoms of opportunistic infections most commonly related with the dynamic of HIV/AIDS. Patients often experienced weight gains as part of an overall pattern of positive response. After 1 day of use there was a moderate level of relief of fever and diarrhoea. After 14 days of use all patients experienced relief of skin lesions, mouth thrush, fever, diarrhoea and tuberculosis. After 90 days of use all

patients experienced relief of all symptoms. After 330 days all patients did not experience any negative symptoms.

Subsequent to finding positive results of Efficacy and Safety/Tolerability in phase I, II & III trials with RECEPTOL® in the US and Africa, the Ministry of Health and Family Welfare, Government of India, under the Pharmaceuticals Research and Development Support Fund, had funded a phase III trial of its efficacy in HIV / AIDS patients coordinated by National AIDS Control Organization (NACO) / Indian Council of Medical Research (ICMR) / Director General Health Services (DGHS) / Drug Controller General of India (DCGI) in consultations with Dr. Pawan Saharan, Chairman, Biomix Network Limited, India at Lokmanya Tilak Municipal Medical College, Sion, Mumbai during October 2005 & October 2006. The objective of this study was to determine the efficacy of a novel dosage form of an oral spray of RECEPTOL® liquid in the HIV infected patients with respect to effect on the HIV viral load, AIDS related clinical symptoms/physical findings, Absolute CD4 cell counts and effect on body weight.

Background of RECEPTOL® Trials in HIV Patients

• Phase I: HIV trial, USA

• Phase II : HIV trial, Nairobi – Kenya

• Phase III: HIV trial, Rwanda for 365 days.

Phase III : Revalidation trial by Government of India on HIV patients

• Jan 12, 2005: Ministry of Health & Family Welfare, approval for the Phase III RECEPTOL

• March 03, 2005: Scientific and Ethics Committee of L. T. M. M. college, Sion approval for clinical trial

• May 11, 2005: ICMR –Toxicology Review Panel Approval

• June 27, 2005: ICMR appointed Dr. Khedkar (NARI, Pune) & Dr. Thatte (clin pharmac, BYL Nair Hospital)as observer for the trial with ICMR recommended protocol.

• Dec 19, 2005: NACO Apex Research Committee approval and funding for Phase III RECEPTOL Trial

• March 30, 2006: Department of Science and Technology funding for the project under PRDSF with recommendation of the President of India

• Study I (2006-07): Accelerated, prospective Phase III efficacy study for RECEPTOL® was conducted for 50 HIV seropositive patients at Lokmanya Tilak Municipal Medical College, Mumbai - Clinical trial registry No. : 2009 000181

• Study II (2007-08): Accelerated, prospective Phase III efficacy study for RECEPTOL® was conducted for 51 HIV seropositive patients at Lokmanya Tilak Municipal Medical College, Mumbai - Clinical trial registry No: 2009 000182

9 STUDY OBJECTIVES

Primary Objective

• **To evaluate the efficacy of RECEPTOL® liquid in HIV/AIDS patients in terms of reduction in HIV viral load and HIV/AIDS related clinical symptoms.**

Secondary Objectives

To determine the effect of oral administration of RECEPTOL® liquid spray on:

• Change in Body Weight of patients

• Absolute CD4 cell count

• Overall Assessment of Efficacy and Safety/Tolerability of RECEPTOL®

10 INVESTIGATIONAL PLAN

Overall Study Design and Plan: Description

• This was a Stand alone, 12-week study undertaken to determine the effect of treatment with RECEPTOL® on HIV viral load and clinical symptoms in 50 subjects with HIV / AIDS. Both Male and Female HIV/AIDS subjects between 18 and 60 years of age who fulfilled the Inclusion and Exclusion Criteria were enrolled for this study. Written Informed Consent from these subjects was obtained prior to their enrollment.

- Stand alone trials were conducted with the product because the drugs of Anti Retroviral therapy are so strong that when given with any other medication, they mask its effect.

• This study was conducted to determine the efficacy of RECEPTOL® liquid spray administered daily for 11 weeks. The study was designed to investigate for the effect of RECEPTOL® therapy on viral load and clinical symptoms and physical findings. Also, to monitor the effect on Absolute CD4 cell counts. The primary endpoints of the study included effect of this therapy on markers of HIV disease including the reduction in HIV viral load and improvement in clinical symptoms. The secondary endpoints included increase in Absolute CD4 cell counts, body weight gain, along with the general well being of the patients.

• Participants were evaluated in the clinic once every week through the first 4 weeks of therapy, and then onwards at every 2 weeks interval for the remaining 8 weeks of the study. Patients were evaluated for clinical and physical symptoms through symptom assessment forms, physical examination, incidence of side effect of treatment and compliance to trial treatment on follow up visits. Blood tests to measure HIV viral load & ABSOLUTE CD4 cell counts were done at baseline and at end of study treatment.

• Absolute CD4 cell count was analyzed by Flow Cytometry while HIV viral load using Polymerase Chain Reaction at NABL and CAP-US Accredited Central Metropolis Laboratory in Mumbai for this trial.

Subject Selection Criteria

• The selection of the subjects for this trial was based on the following Inclusion & Exclusion criteria.

INCLUSION CRITERIA

• Male and Female Subjects between 18 and 60 years of age.

• Documentation of HIV infection by any licensed ELISA test, disease contracted heterosexually (no drug abuse) preferably within six months.

• **Subjects having Absolute CD4 count greater than 100 cells/cmm.**

• Subjects will have measurable HIV viral load.

• Subjects willing to give informed consent for their stay in the hospital and / or follow up visits.

EXCLUSION CRITERIA

• Pregnant or nursing women, women of childbearing potential not using an adequate method of birth control.

• Subjects with kidney failure with serum creatinine greater than 1.5 mg/dL.

• A history of Hepatic Cirrhosis.

• Congestive Heart Failure (CHF).

• Current alcohol or substance abuse that could interfere with patient compliance.

• Organ transplant recipient.

• Pre-existing Uncontrolled Seizure Disorder.

• **Subjects using long term systemic corticosteroids, Immuno-Suppressive and ART.**

10.2 Treatment Procedures

RECEPTOL® liquid spray used in the study was a Colostrum product, containing natural microscopic molecules of Radha108 of 800 – 1200 Dal molecular weight (below 2000 DaL that enable to cross bbb- Blood brain barrier) and PRPs consisting of oligoribonucleotides attached to a peptide molecule. RECEPTOL® was manufactured by Biomix Network Ltd., Mumbai by protein fractionation and ultra nano filtration technology the only nanotechnology based plant in India. Eligible patients were evaluated for medical history, physical examination, blood and urine tests, and other tests as determined by the Principal Investigator. Patients had received RECEPTOL® liquid in pump spray form and were taught to self-administer the medication. The Frequency of dose administration was 6 times per day at every 4 hour intervals. Each single administration consisted of 5 sprays directly on the buccal mucosa (inner cheek). The patients were advised to gargle the medication in the mouth for 1 min before swallowing it. Each pump of the spray device delivered 0.75 ml of RECEPTOL® liquid. The trial treatment as described above was continued for a period of 12 consecutive weeks.

Assessment Schedule

Study Activities	Screening (Week 0)	Visit 1 (Week 1)	Visit 2 (Week 2)	Visit 3 (Week 3)	Visit 4 (Week 4)	Visit 6 (Week 6)	Visit 8 (Week 8)	Visit 10 (Week 10)	Visit 12 (Week 12)
Inclusion/Exclusion Criteria	X								
Patient Informed Consent	X								
Relevant Medical History	X								
Physical And Systemic Examination	X								
Demography	X								
Chest X-ray And ECG	X								
Absolute CD4 Cell Count And HIV Viral Load Examination	X								X
Clinical Symptoms and Physical Findings		X	X	X	X	X	X	X	X
Body Weight	X	X	X	X	X	X	X	X	X
Overall Assessment Of Efficacy And Safety/Tolerability									X
Study Medication Dispensed		X	X	X	X	X	X	X	
Adverse Events			X	X	X	X	X	X	X

Compliance

• Each patient self administered 4 sprays (each measuring 0.75 ml of the liquid) of RECEPTOL® liquid, daily, at every 4 hour intervals. They were advised to have a 6 hrs sleep, at a time, to facilitate 6 hourly medications and were also advised to follow a regular daily exercise.

• Patients were instructed to spray the study drug in mouth and allow it to circulate in mouth for 1 minute and then swallow it.

• Patients were asked to follow a well balanced diet of 40% Carbohydrates, 30% Protein, 30% Fats and Oils, to drink plenty of clean fresh water and avoid any such food that may cause increased gastric acidity.

Blinding/Randomization Technique

• Not Applicable

Assessment of Efficacy and Safety Criteria

• Blood Samples to assess the HIV viral load and Absolute CD4 cell count were collected at baseline (Week 1) and end of treatment (Week 11).

• HIV viral load was assessed on basis of PCR Diagnosis while Absolute CD4 cell counts were based on Flow Cytometry System Analysis.

• Clinical symptoms and Physical Findings which included HIV related Fatigue/Malaise, Diarrhoea, Nausea, Vomiting, Fever, Cough, Paraesthesia Sleep Disturbance, Skin Rash, Herpes Zoster, Lymphadenopathy, Hair Changes, Oral Thrush, Leukoplakia, Liver Enlargement, Spleen Enlargement, Weight of Patient and Tuberculosis were assessed using Symptom Assessment Form which was recorded in patients every visit.

• Safety parameters were assessed by measuring the number of Adverse and Serious Adverse Events.

• Overall Assessment of Efficacy and Safety/Tolerability was made by both, the treating Physician and the participating patients.

Statistical Methods Used

• The primary efficacy parameter i.e. HIV viral load was analyzed statistically by using Wilcoxon Signed rank test at 5% level of significance. A median change in this parameter was observed from Baseline to Week-12 (End of Treatment).

• While HIV related clinical symptoms and physical findings were calculated using chi-square test at 5% level of significance reporting these symptoms.

• Secondary efficacy parameters Absolute CD4 cell count was analyzed by using Wilcoxon Signed rank test at 5% level of significance.

• Secondary efficacy parameters including body weight gain was analyzed using paired sample t-test at 5% level of significance.

• Overall Assessment of Efficacy & Safety/Tolerability by Physicians & Patients was calculated by using frequency distribution and percentage.

11 TRIAL SUBJECTS

• A total of 74 patients were enrolled in this study, out of which 2 patients did not fulfill the given inclusion criteria, 22 out of town patients dropped out from this study due to not being able to travel from their villages. Therefore, at the end of study, pre and post treatment data of 50 patients mentioning clinical symptoms and biochemical profile including Absolute CD4 cell count and HIV viral load were available for analysis.

(Total no. of Patients Enrolled = 74 and Analyzed = 50)

12 STUDY RESULTS

Study Details

Study Details	No. Of Patients (%)
No. Of Patients Enrolled	74 (100%)
Inclusion Criteria Not Fulfilled	02 (2.70%)
Evaluable	72 (97.30%)

No. of out of town Patients Dropped Out	22 (29.73%)
No. of Patients Analyzed	50 (67.57%)

A total of 74 patients were enrolled in this study, out of which 2 (2.70%) patients did not fulfill the given inclusion criteria, 22 (29.73%) patients dropped out from this study. Thus, 50 (67.57%) patient were considered for statistical analysis.

Table of Demographic of Subjects Enrolled in the Trial

Demographic		**Statistics**	**Result**
Age (years)		Mean	34.33
		SD	8.87
		Range	20-56
Sex	Male	N (%)	28 (56%)
	Female	N (%)	22 (44%)
Weight (kg)		Mean	50.48
		SD	10.97
		Range	30-75

In this study group age of patients were ranging from 20 to 56 years with mean age 34.33. Mean weight of the patients were 50.48 Kg. Out of the total cases, 56% were male and 44% were female.

Efficacy Evaluation

Primary Efficacy Results:

Table of Change in HIV Viral Load from Baseline to Week-12

Sr. No	Parameter	Before	After 11 weeks	p–value
	Log of HIV-1, RNA (N=34)	5.11(0.090)	4.103(1.32)	< 0.001
1.	Median	206057	25280	< 0.001
2.	25th Percentile	62884	1665	
3.	75th Percentile	508038	87511	

HIV Viral Load: At the end of 11 weeks treatment with RECEPTOL® the median showed significant difference as compared to baseline (p <0.001). The baseline value of median 206057 and at the end of 11 weeks treatment the median value was 25280.

Table Showing Number of Patients Showing Various Clinical and Physical Symptoms (Incidence) and Its % Frequency at Baseline and Week 11.

Duration	Nausea	Vomiting	Disturbed Sleep	Tuberculosis	Skin Rash
Week-1	8(16.0%)	7(14.0%)	13(26.0%)	6(12.0%)	7(14.0%)
Week-2	3(06.0%)	3(06.0%)	8(16.0%)*	00(00%)	2(04.0%)*
Week-3	2(04.0%)*	2(04.0%)	3(06.0%)*	00(00%)	1(02.0%)*
Week-4	1(02.0%)*	1(02.0%)*	1(02.0%)*	00(00%)	00(00%)
Week-5	00(00%)	00(00%)	00(00%)	00(00%)	00(00%)
Week-6	00(00%)	1(02.0%)	00(00%)	00(00%)	00(00%)
Week-7	00(00%)	00(00%)	1(02.0%)	00(00%)	00(00%)
Week-8	00(00%)	00(00%)	1(02.0%)	00(00%)	00(00%)
Week-9	00(00%)	00(00%)	00(00%)	00(00%)	00(00%)
Week-10	00(00%)	00(00%)	00(00%)	00(00%)	00(00%)
Week-11	00(00%)	00(00%)	00(00%)	00(00%)	00(00%)
Week-12	00(00%)	00(00%)	00(00%)	00(00%)	00(00%)

By Chi-Square Test *** p<0.05 Significant**

Duration	Fatigue	Diarrhoea	Fever	Herpes Zoster	Cough
Week-1	44(88.0%)	9(18.0%)	12(24.0%)	6(12.0%)	14(28.0%)
Week-2	32(64.0%)	5(10.0%)	3(06.0%)	2(04.0%)	10(20.0%)
Week-3	26(52.0%)*	1(02.0%)*	6(12.0%)	1(02.0%)*	6(12.0%)*
Week-4	17(34.0%)*	1(02.0%)*	1(02.0%)*	00(00%)	3(06.0%)*
Week-5	8(16.0%)*	00(00%)	2(04.0%)*	00(00%)	4(08.0%)*
Week-6	1(02.0%)*	00(00%)	1(02.0%)*	00(00%)	1(02.0%)*
Week-7	2(04.0%)*	00(00%)	00(00%)	00(00%)	3(06.0%)
Week-8	1(02.0%)*	00(00%)	00(00%)	00(00%)	2(04.0%)*
Week-9	2(04.0%)*	00(00%)	1(02.0%)*	00(00%)	2(04.0%)*
Week-10	1(02.0%)*	00(00%)	00(00%)	00(00%)	00(00%)
Week-11	00(00%)	00(00%)	00(00%)	00(00%)	00(00%)
Week-12	00(00%)	00(00%)	00(00%)	00(00%)	00(00%)

By Chi-Square Test *** p<0.05 Significant**

All the Clinical Symptoms & Physical Findings had reduced from Week 2 onwards which disappeared during the 11 weeks of treatment. These reductions were statistically significant ($p < 0.05$).

Figure 1: Reduction in Number of Patients with Diarrhoea During the 11 weeks Trial Treatment with RECEPTOL® **18 % of the total study cases had Diarrhoea at basal and after treatment from 5th week onwards all the patients had relief from Diarrhoea. (Figure 1)**

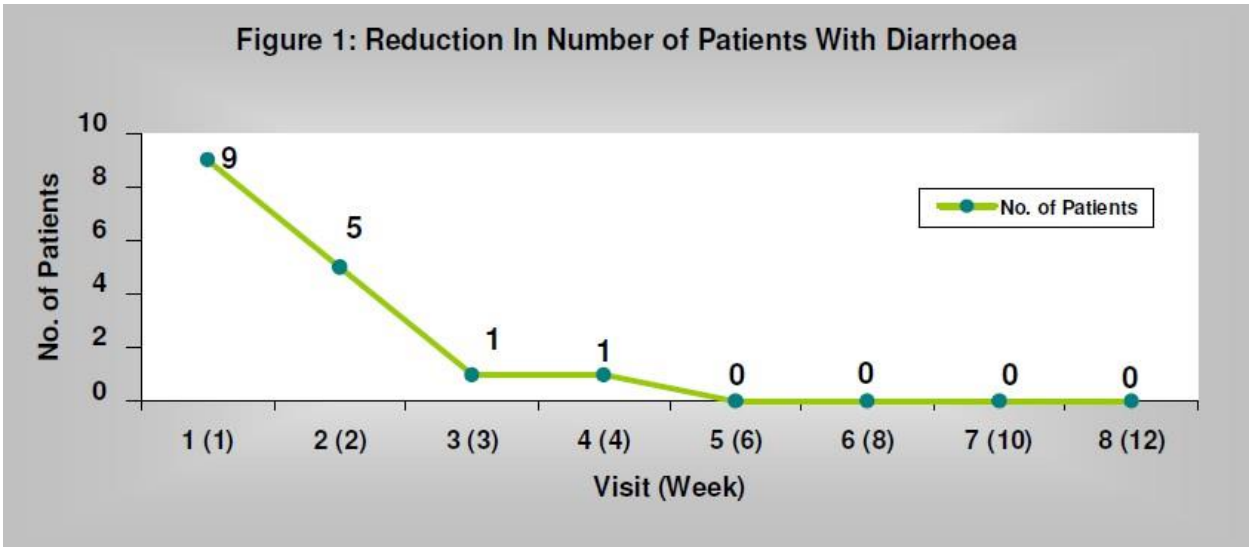


Figure 4: Reduction in Number of Patients with Fever during 11 weeks Trial Treatment with RECEPTOL®

Fever was reported by 24 % of total study cases at basal and from 7th week onwards not a single patient had fever with significant fall started 4th week onwards. (Figure 4)

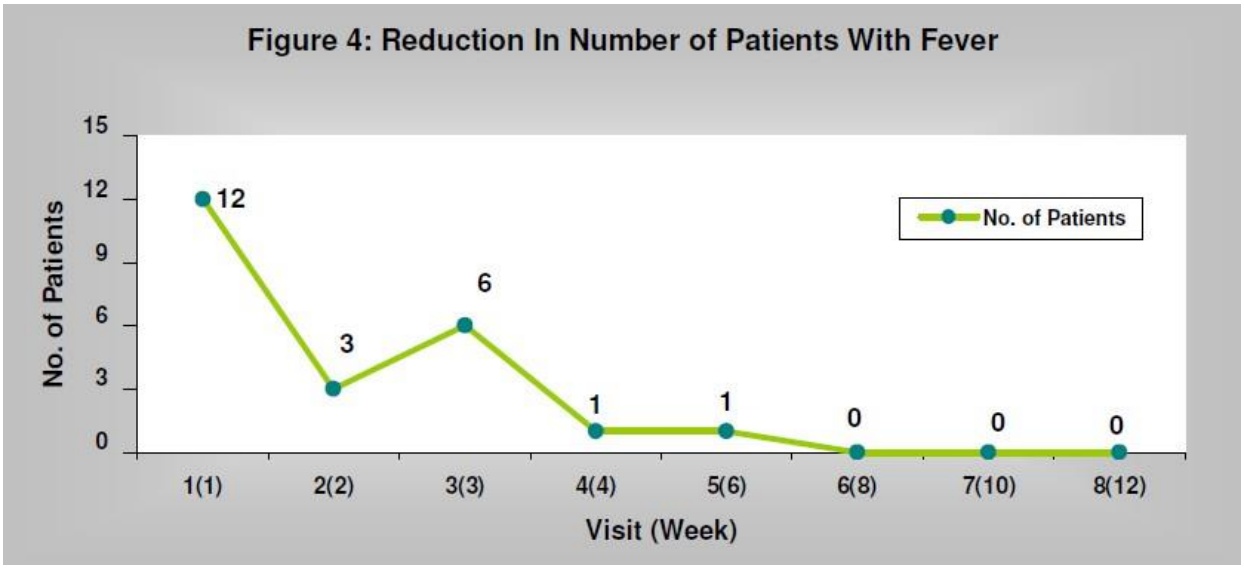


Figure 5: Reduction in Number of Patients with Cough during 11 weeks Trial Treatment with RECEPTOL®

28 % of the total study cases had a symptom of Cough at basal which had significant fall from 3rd week onwards and all improved 10th week onward (Figure 5).

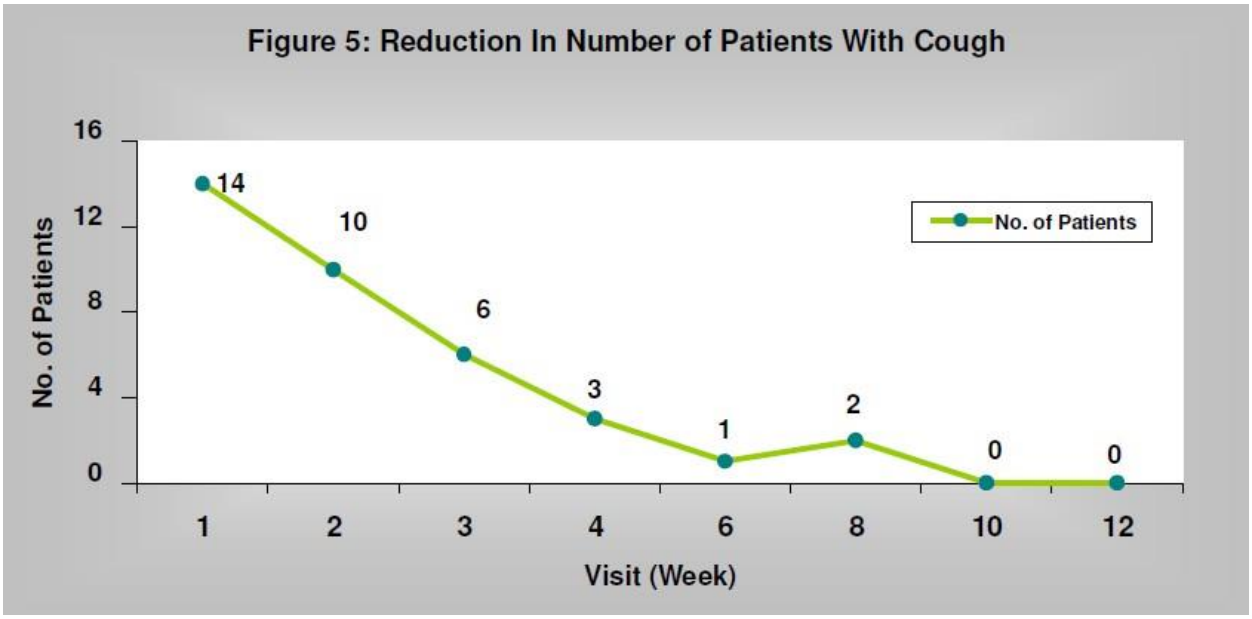


Figure 6: Reduction in Number of Patients with Fatigue/Malaise During 11 weeks Trial Treatment with RECEPTOL®

88 % of the total study cases had symptoms of Fatigue/Malaise at baseline. After treatment of RECEPTOL® at the end of 2nd week proportion of symptoms of fatigue had a significant fall from baseline. After 6th week onwards only one or two patients had Fatigue/Malaise (Figure 6).

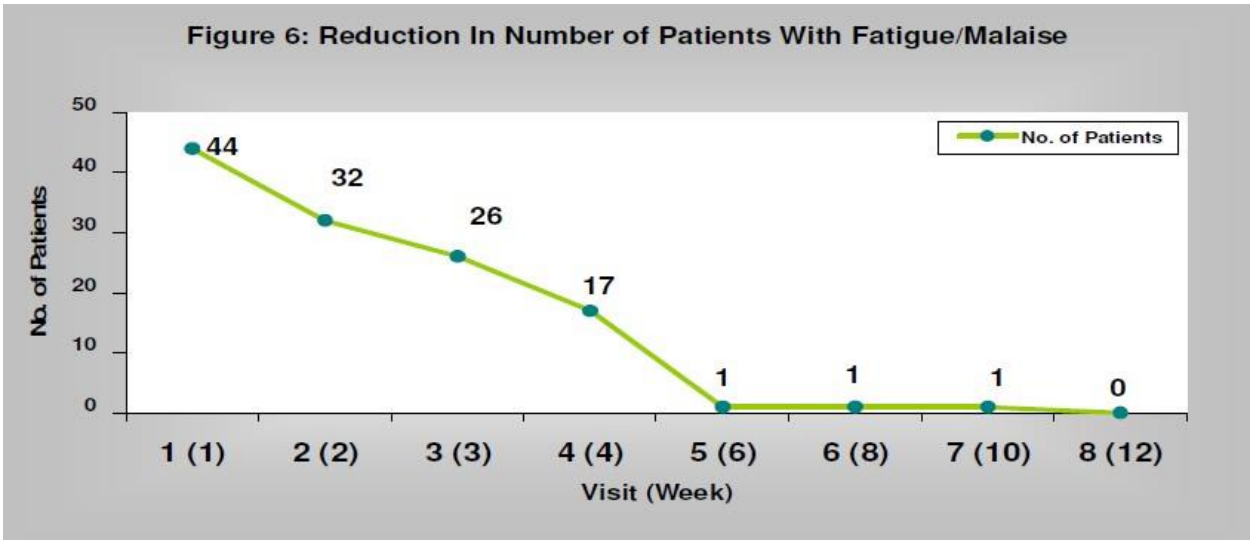


Figure 7: Reduction in Number of Patients with Disturbed Sleep During 11 weeks Trial Treatment with RECEPTOL®

26 % of the total study cases had HIV related Disturbed Sleep at baseline and after treatment from 5th week onwards all the patients had relief from Disturbed Sleep. (Figure 7)

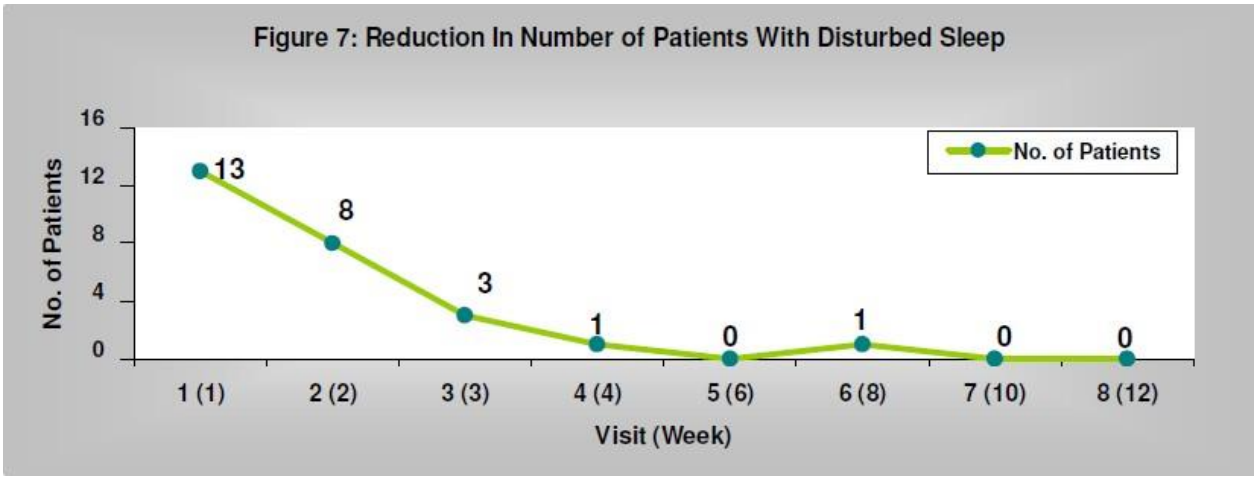


Figure 8: Reduction in Number of Patients with Skin Rash During 11 weeks Trial Treatment with RECEPTOL®

14% of the total study cases had HIV related Skin Rash at baseline and after treatment from 4th week onwards all the patients had relief from Skin Rash. (Figure 8)

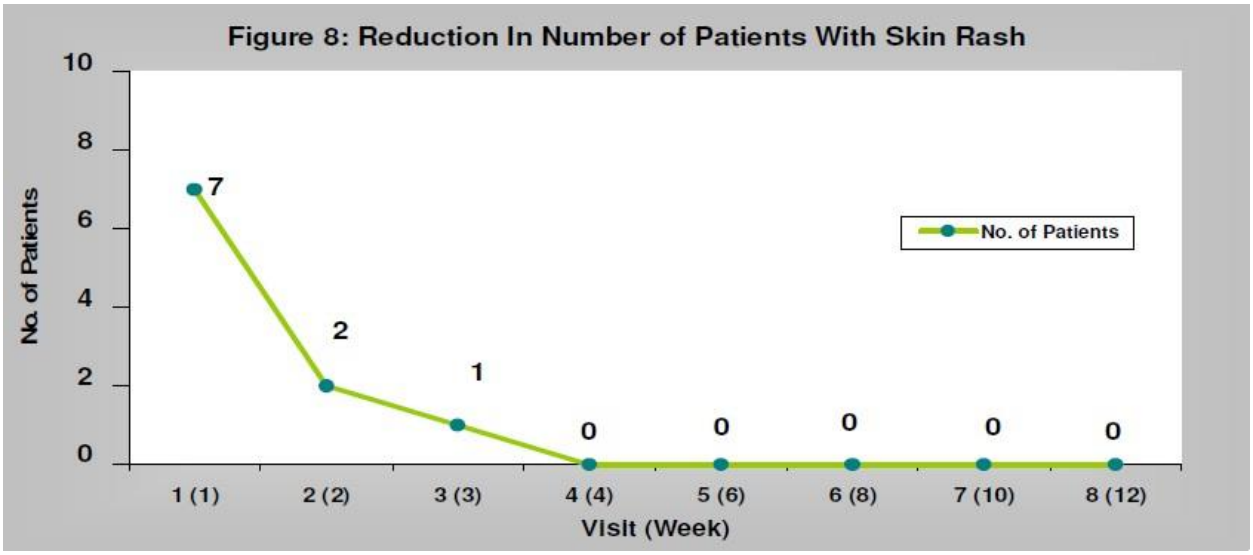


Figure 9: Reduction in Number of Patients with Herpes Zoster during 11 weeks Trial Treatment with RECEPTOL®

12% of the total study cases had HIV related Herpes Zoster at baseline and after treatment from 4th week onwards all the patients had relief from Herpes Zoster. (Figure 9)

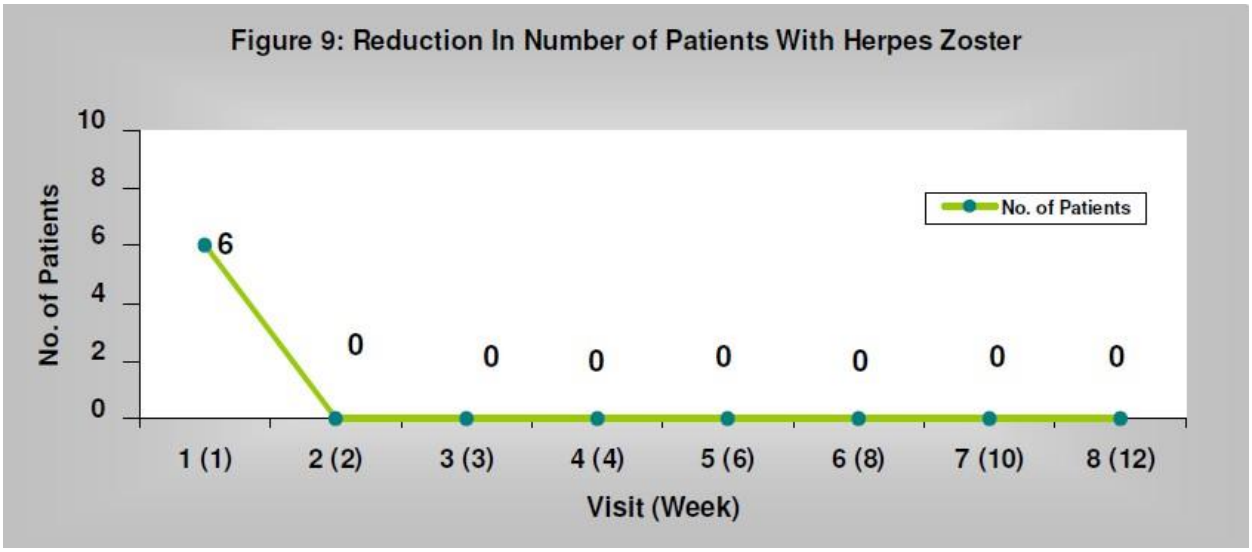
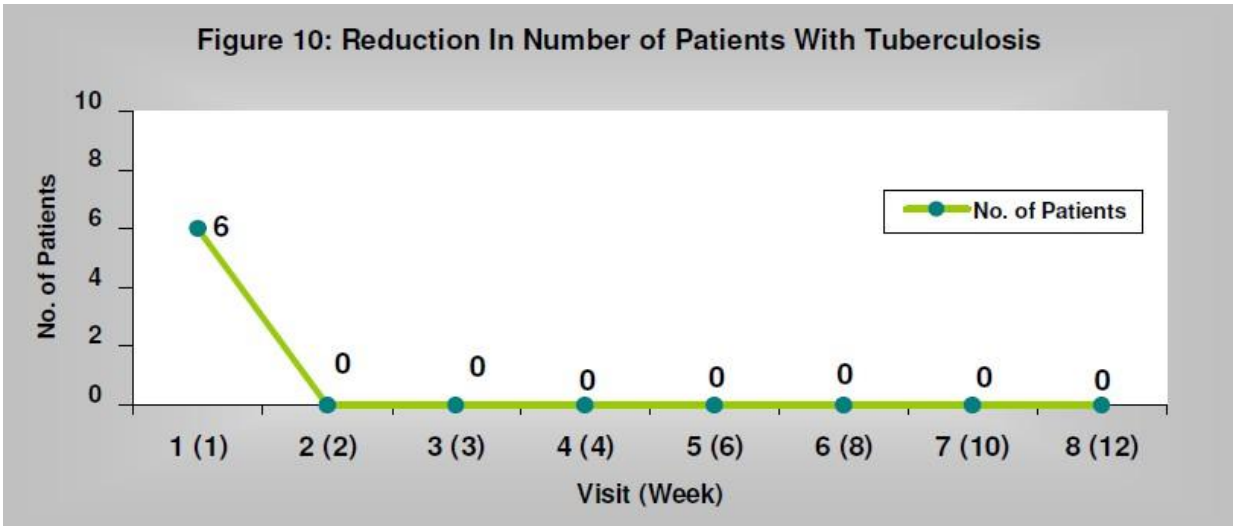


Figure 10: Reduction in Number of Patients with Tuberculosis During 11 weeks Trial Treatment with RECEPTOL®

12% of the total study cases had HIV related *Tuberculosis* at baseline and after treatment from 2nd week onwards all the patients had relief from Tuberculosis. (Figure 10)



Secondary Efficacy Results:

Table of Change in Mean Absolute CD4 Count at Week-11

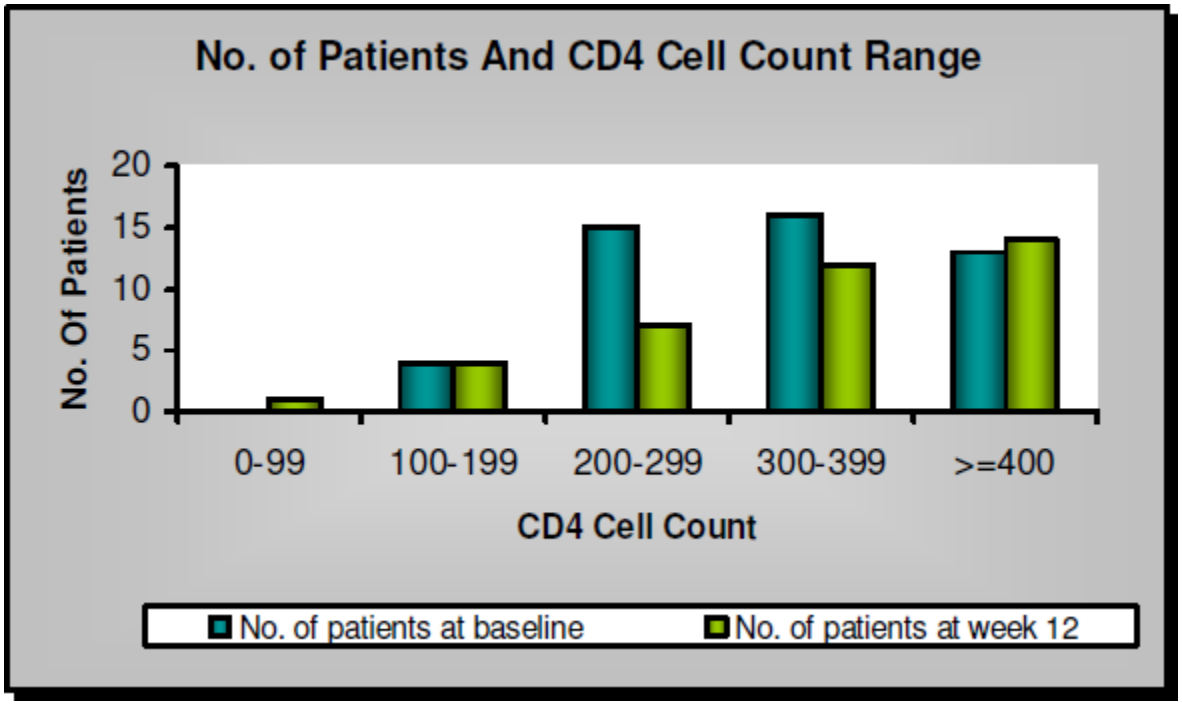
Sr. No	CD4 count N=48	Before	After 11 weeks	p–value
	Median	312.5	363.5	0.06
	25th Percentile	275.5	294.2	
	75th Percentile	430	435	

The above table reveals that median of absolute CD4 count was 312.5 at baseline. At the end of the study at Week 11 median of absolute CD4 count was 363.5. Therefore the average CD4 counts showed an increase by 51 (Median counts from 312 to 363). This is of borderline statistical significance (p=0.06).

Absolute CD4 Count:

Absolute CD4 cell count was available for all 50 patients with pre and post treatment values. There was an increase in Absolute CD4 count in 26 (52%) patients. Absolute CD4 cell count range with number of patients at baseline and at the end of study is shown in Figure 11.

Figure 11: No. Of Patients and Absolute CD4 Cell Count Range



*** As the Absolute CD4 Cell counts chart shows patients who were within the range of 100 to 199 and needed ART treatment, still were given stand alone RECEPTOL® therapy and recovered satisfactorily without ART**

12.2.6 Table Showing Comparison of Mean Body Weight of Subjects at Baseline (Week 1) With End of Treatment Measurements.

Duration	Weight (Mean ± SD)	Mean Weight Gain from Baseline
Week-1	50.48 ± 10.97	00
Week-2	50.77 ± 11.26	0.29
Week-3	51.38 ± 10.94	0.9
Week-4	52.33 ± 10.73	1.85
Week-6	53.89 ± 11.17*	3.41
Week-8	54.59 ± 10.89*	4.11
Week-10	55.44 ± 11.07*	4.96
Week-12	55.21 ± 09.42*	4.73

By Paired Sample t-test $p<0.05$ Significant

Mean body weight of patients measured at end of 11 weeks treatment showed a significant increase when compared with those measured at baseline. ($p< 0.05$)

Figure 12: Effect of 11 weeks Treatment with RECEPTOL® on Mean Body Weight of Patients.

Weight monitored on every visit showed significant gain in all 50 HIV patients with mean weight gain of 4.73 kg after 11 weeks of RECEPTOL® therapy (p< 0.05). (Figure 12)

Safety Evaluation

• Safety and tolerability assessments consisted of monitoring and recording all Adverse Events and Serious Adverse Events. All patients tolerated RECEPTOL® well with no side effects. Even the Milk allergies for certain people caused by the large milk proteins, primarily casein, and to a lesser extent the Immunoglobulin. These proteins are completely removed from the RECEPTOL® during nano-filteration process using molecular weight exclusion columns As RECEPTOL® is a natural food supplement derived from mammalian Colostrum (the first few milk after the birth of child calf), it was found to be safe for human consumption.

Overall Assessment by Investigator & Patient

Table of Principal Investigators Assessment for Efficacy of Trial Drug

Investigator's comment for Efficacy	N*	Percentage	Cumulative Frequency	Cumulative Percentage

Very Good	**03**	**05.66**	**03**	**05.66**
Good	**29**	**54.72**	**32**	**60.38**
Satisfactory	**16**	**30.19**	**48**	**90.57**
Others	**05**	**09.43**	**53**	**100**

***N stands for Number of patients in the study**

Table of Principal Investigators Assessment for Safety/Tolerability of Trial DrugTreatment

Investigator's comment for Safety/Tolerability	***N***	**Percentage**	**Cumulative Frequency**	**Cumulative Percentage**
Very Good	25	47.17	25	47.17
Good	25	47.17	50	94.34
Others	3	05.66	53	100

Table of Patients Assessment for Efficacy of Trial Drug Treatment

Patient's feedback for Efficacy	***N***	**Percentage**	**Cumulative Frequency**	**Cumulative Percentage**
Very Good	01	1.89	01	01.89
Good	2541	77.36	42	79.25
Satisfatory	307	13.21	49	92.46
Others	04	7.54	53	100

Conclusion of Principal Investigator and patients Assessment

• **According to Principal Investigators Assessment:** 90.57% of the patients showed Very Good, Good and Satisfactory results for efficacy of the trial drug treatment.

• **According to Investigators Assessment:** 94.34% of the patients showed Very Good and Good results in terms of the safety/tolerability of the trial drug treatment.

• **According to Patients Assessment:** 92.46% of the patients showed Very Good, Good and Satisfactory results for efficacy of the trial drug treatment.

• **According to Patients Assessment:** 79.25% of the patients showed Very Good and Good results for the safety/ tolerability of the trial drug treatment while 15.09% of the patients experienced no side effects.

13 DISCUSSION AND OVERALL CONCLUSION

• A total of 74 patients were enrolled in this study, out of which 2 patients did not fulfill the given inclusion criteria, 22 out of town patients dropped out from this study due to not being able to travel from their villages, Therefore, at the end of study, pre and post treatment data of 50 patients mentioning clinical symptoms and biochemical profile including HIV viral load and Absolute CD4 cell count were available for analysis.

• **Sample size for this stand alone monotherapy with RECEPTOL® only was calculated by following recommendations as per the End-Points used in any WHO study :**

1) Institutional Review Board of LTMMC & LTMG Sion Hospital consisting of Scientific Committee, Ethics Committee & Biostatistics Department of Sion Hospital

2) National Institute of Medical Statistics (Indian Council of Medical Research)

3) All India Institute of Medical Sciences (AIIMS) – Biostatistics Department

4) Ministry of Health & Family Welfare notification no. F-207 dated 12/01/05

• Out of the total of 50 subjects, 28 (56%) were Male and 22 (44%) were Female having average weight 50.48 kg with SD 10.97, average age 34.33 years with SD 8.87 with the range of 20-56 years.

• At the end of 12-Week Treatment (end of the study) with RECEPTOL® showed **significant change (reduction) in HIV viral load** based on PCR Diagnostic Test.

• At the end of 12-Weeks Treatment (end of the study) with RECEPTOL®, **median of HIV Viral load showed a significant change (p<0.001) from baseline** as evident in the **statistical analysis which was done by Dept. of Biostatistics, AIIMS.**

• At baseline, 88% of Patients had **Fatigue/Malaise** which became asymptomatic after 6th week of treatment with RECEPTOL®.

• HIV related **Diarrhoea** was reduced in all patients from 5th Week onwards with significant reduction from 3rd Week

• **Nausea** disappeared from 5th Week onwards with significant fall from 3rd Week onwards. HIV related **Vomiting** had significant fall after 4th Week and all patients became asymptomatic after 7th Week onwards**.**

• Significant fall in **Fever** and related symptoms was observed in all HIV patients after 4th week and became asymptomatic after 7th week onwards.

• HIV related **Cough** had a significant fall from 3rd week onwards and all patients became asymptomatic from 10th week onwards**.**

• **HIV related Tuberculosis patients became asymptomatic from 2nd week onwards.**

• HIV related **Disturbed Sleep** patients had a significant improvement after 2 weeks of treatment and became asymptomatic after 5th week.

• HIV related **Skin Rash** had a significant fall at the end of 2nd week and all patients reported no rashes from 4th week onwards.

• HIV related **Herpes Zoster** had a significant fall at the end of 3rd week and became asymptomatic in all patients after 4th week with the treatment RECEPTOL®.

• 11 weeks continued treatment with RECEPTOL® resulted in a significant increase in Absolute CD4 cell count with a reduction in HIV viral load. The results also showed a marked improvement in HIV Related Clinical Symptoms and Physical Findings and all patients were relieved of their symptoms by the treatment with RECEPTOL®.

• At the end of 12-Week Treatment (end of the study) with RECEPTOL®, median of **Absolute CD4 counts showed p<0.06 based on Flow Cytometry Analysis**. This is of borderline statistically significant.

• **All patients showed significant gain in Body Weight during 12 Week trial therapy With RECEPTOL® with an average gain of 4.73 kg, range of variation 3 - 7 kgs**.

• There was a marked improvement in HIV related clinical symptoms and many patients became asymptomatic at the end of 3 weeks therapy ($p < 0.05$).

• The 11 weeks trial treatment with **RECEPTOL® was well tolerated by all 50 patients and no patient experienced any Adverse or Serious Adverse Events** .

• The **overall results** obtained from this trial prove that continued treatment with RECEPTOL® Oral Spray for 12 consecutive weeks resulted in a **significant decrease in HIV viral load and increase in the Absolute CD4 cell count** along with a significant gain in body weight leading to relief of symptoms in all the 50 HIV/AIDS patients studied.

• **As per the previous international studies of Phase I, II & III trials conducted in USA & Africa, RECEPTOL® showed similar clinical efficacy & safety in HIV Patients** .

• Thus, RECEPTOL®, a natural Nano-Informational Peptides (RADHA1081-100) and Proline Rich Polypeptides (PRPs) derived from the Bovine Colostrum holds good promise for a safe and effective alternative treatment for HIV Patients across all age group.

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