

PHASE IV

CLINICAL STUDY TO EVALUATE EFFICACY OF IMMUNE-MODULATOR HOMEOPATHY DRUG 'CANOVA' IN HIV/AIDS PATIENTS

By: Unison Medicare & Research Centre Pvt. Ltd.

COMPREHENSIVE REPORT ON EFFICACY OF 'CANOVA'

Primary Objective:

1. Does Canova improve the quality of life by being a Homeopathic immunomodulator in immunocompromised patient given alone?
2. Does Canova improve the immune-status by being a Homeopathic immunomodulator in HIV/AIDS patients who have become resistant to Anti-Retroviral Treatment (ART)?

Secondary Objectives:

1. To test the efficacy of CANOVA in improving quality of life in patients of HIV/AIDS.
2. To study the efficacy of CANOVA in elevating the number of CD4 + cells or maintaining the same in HIV/AIDS patients, thus showing its immunomodulator activity
3. To test the efficacy of CANOVA in preventing the onset of Opportunistic Infections in HIV/AIDS patients.
4. To test effect of CANOVA on the plasma viral load in patients of HIV/AIDS

ELIGIBILITY CRITERIA:

- a) HIV-1 confirmed patients: Patients with established HIV infection diagnosed by one ELISA + 2 spot or three different spot or ELISA/Spot + Confirmation by the Western Blot;
- b) Patients from either sex
- c) Age > 18 years.
- d) CD4 count 150 to 200 cells/ μ litre in ART-naïve patients (not on ART)
- e) Clinical, Immunological and/or Virological failure in case of patients already on ART
In this group ART resistant patients even with very poor CD4 counts were included
- f) Signed informed consent document on file
- g) Male/ female patients with reproductive potential must use approved contraceptives
- h) Estimated life expectancy of > 4 weeks.
- i) Patient compliance and geographic proximity that allow adequate follow up.

EXCLUSION CRITERIA:

- a) Neoplasms affecting HIV patients
- b) Patients having a positive pregnancy test or are breast-feeding?
- c) Patients suffering from other chronic disorders other than related to HIV
- d) Opportunistic Infections in patients not on ART
- e) Previous use of Canova
- f) Known hypersensitivity to Canova

MATERIALS AND METHODS:

The study population included 30 patients who were diagnosed to have HIV-1 infection attending Unison Medicare & Research Centre, an ISO 9001:2000 Certified Comprehensive HIV care clinic in Mumbai, India. ART-Naïve patients who had CD4 count between 150 and 200 (+/-10%) were enrolled in the study. Those patients who were on ART, but have developed clinical or immunological or virological resistance to ARVs were also enrolled in the study.

This was a two-arm study:

1. Canova alone
2. Canova + ART

These two groups were compared and analysed against a control group of ART-Naïve patients who are asymptomatic and whose absolute CD4 were between 150 to 200 cells, from the follow-up records of UMRC from comparable population.

Study Discontinuation

- Investigator decision to withdraw the patient from the study
- Any patients during this study show acute disease non-related to HIV/AIDS.
- Any patient who stops treatment for >5 days in the six-month period.
- Patient withdraws consent.
- Patient is noncompliant with study procedures.

Recruitment:

We recruited a total of 30 HIV+ patients; of which finally 22 (18 male + 4 female) patients completed the full study protocol till the end. The study protocol including inclusion-exclusion criteria, follow-up interval, requisite laboratory check-up etc. was approved by an Independent Ethical Committee headed by a prominent public representative and former Sheriff of Mumbai Mr. Kiran Shantaram. An informed consent was obtained from each subject fulfilling the requisite criteria.

Of the 30 patients 22 followed regularly and taken for study.

Of the eight dropouts 3 were female and 5 were male.

One of them had developed hypersensitivity reaction.

One has developed carcinoma

Two were wrongly put on canova so excluded from treatment.

Two were not following regularly, or taking adequate/irregular treatment

Two are expected to come for follow-up tests in the near future.

Dosage: Canova drops were administered at the dose of 10 drops 3 times daily, sublingually. The 10 drops of Canova is equivalent to (50µl/Kg/Body weight). The patients were explained to take drops after giving 15 succussions (strikes) sub-lingual for dynamisation of the study drug as per homeopathic principle. The document of the Canova suggests that the dynamisation is very important as after succussion the microphage activity increases to almost double.

METHODOLOGY:

Each patient was explained of the purpose of the study and the need for cooperation was emphasised. The principal investigator of the project at the UMRC had personally interviewed and examination the study patients. Interviews were conducted according to the prepared proforma to elicit the information about the demographic profile, the year of diagnosis of HIV, clinical history with emphasis on opportunistic infections. Only those patients who satisfied the inclusion and exclusion criteria were recruited in the study and analysis.

The patients were regularly followed at two-monthly interval for physical check-up, assessing any adverse effects, opportunistic infections and for Laboratory check-up as per protocol.

During the routine follow-up CBC/HB%/ESR; LFT; Urine-Routine tests were done.

Similarly CD4/CD8 counts were assessed at recruitment and then at two monthly intervals using Becton Dickinson FacsCount system, which is supposedly a gold-standard for CD4/CD8 testing.

Montoux Test and X-Ray chest were done at recruitment and at day 180.

HIV RNA levels (Viral Load) were assessed using Roche Amplicor HIV-1 Monitor Quantitative PCR Assay, Version 1.5 on Cobas Analyser, at recruitment and day 180.

BASE LINE

Clinical evaluation

Physical evaluation

Hemogram, LFT, Chest X-ray, Montoux

Specific test: CD 4/CD8 counts and VL

AT 2 MONTH

Clinical evaluation

Physical evaluation

Laboratory test except X-ray, Mx and VL

AT 4 MONTHS

Clinical evaluation

Physical evaluation

Laboratory test except X-ray, Mx and VL

AT 6 MONTHS: Conclusion of study:

Clinical evaluation

Physical evaluation

Hemogram, LFT, X-ray Chest, Montoux

Specific test: CD 4/CD8 counts and VL

EVALUATION:

1. Clinical findings .thorough careful physical examination and weight.
2. Occurrence of Opportunistic Infections
3. Occurrence of Adverse Effects to the study drug
4. Laboratory findings: Hemogram, LFT, Chest X-ray.
5. Specific tests like CD4+T Cells count and Plasma RNA/Viral load (VL)

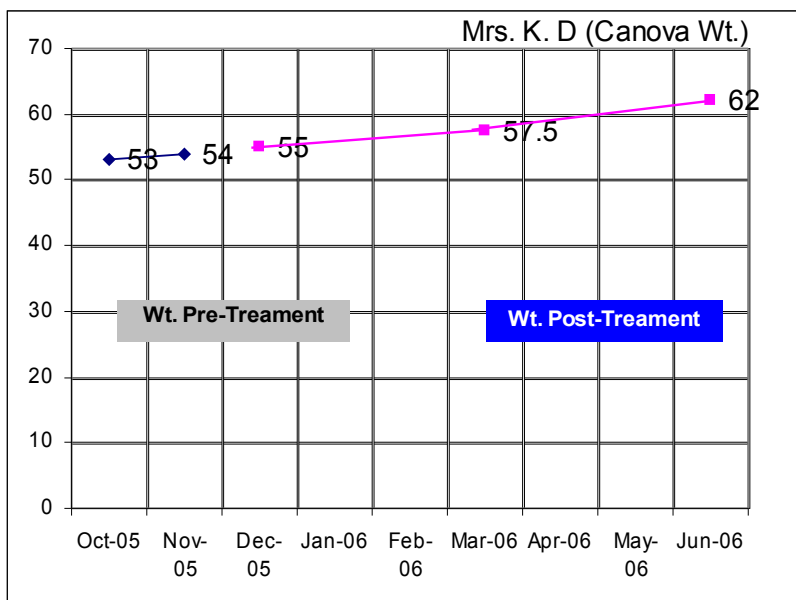
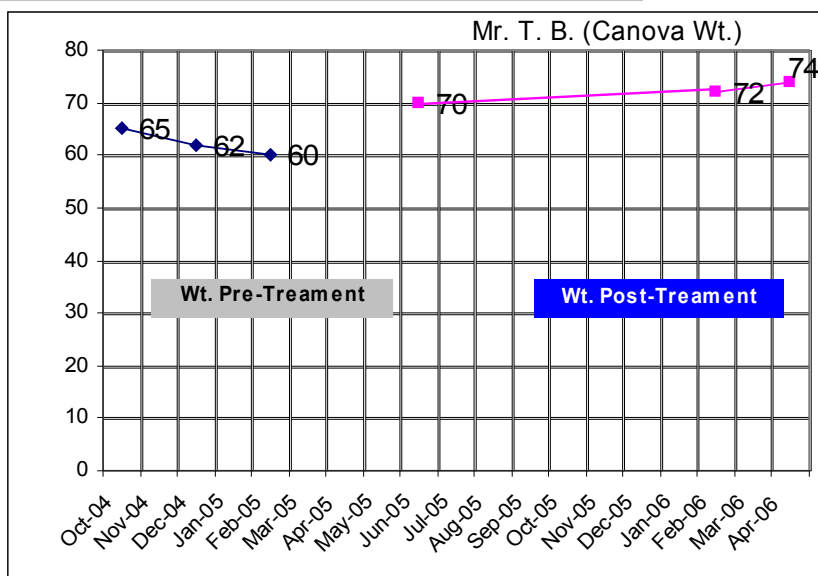
Analyses of results:

Haemoglobin:

HB gm%	Day '0'	Day 180	Difference	Comment
Canova	12.9%	13.4%	0.5%	Insignificant
ART+Canova	11.9%	12.6%	0.7%	Insignificant

Weight in k.g.:

Weight	Day 0	Day 180	Difference	Comment
Canova	55.27	58.39	3.11	Significant
ART+Canova	55.5	58.26	2.76	Significant

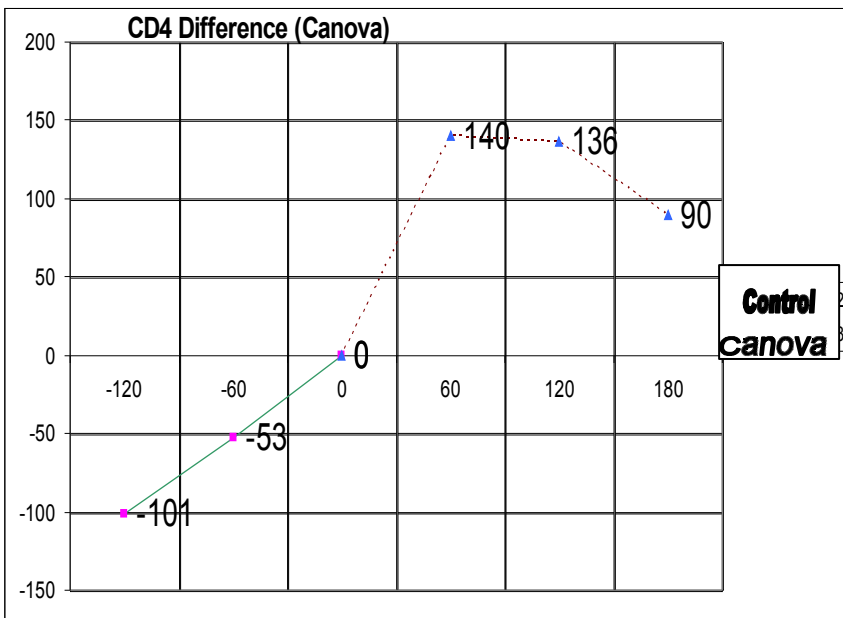
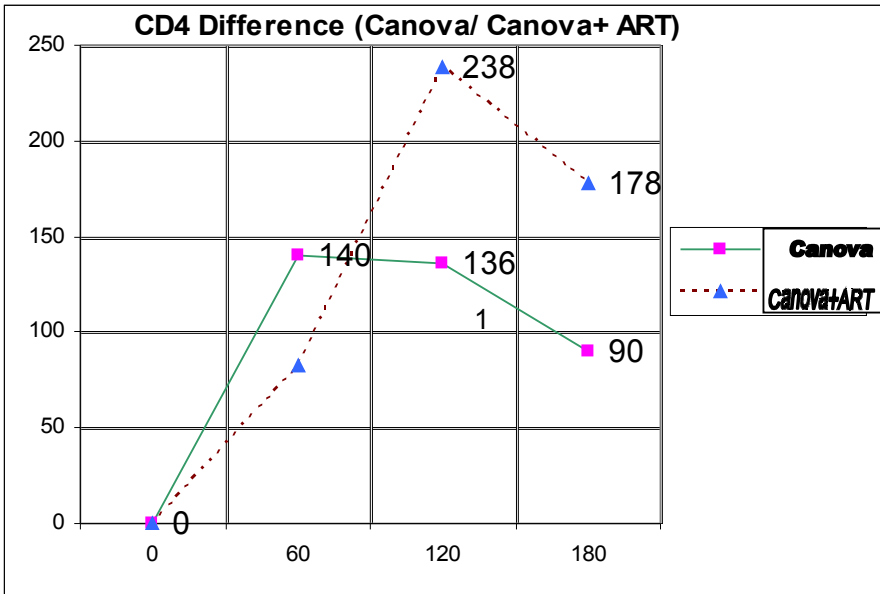


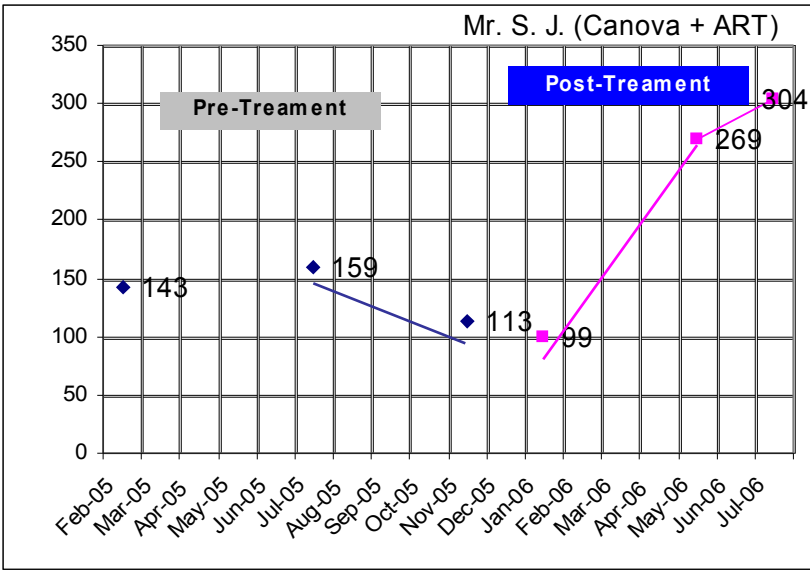
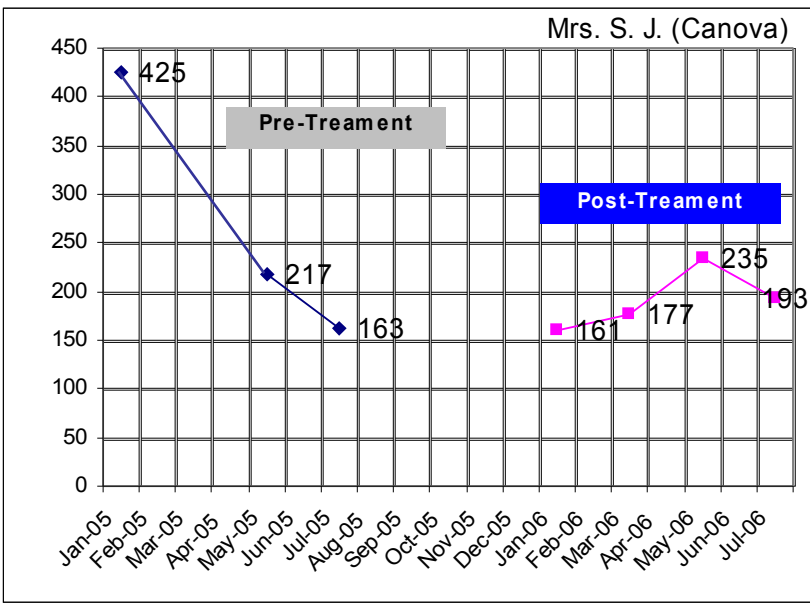
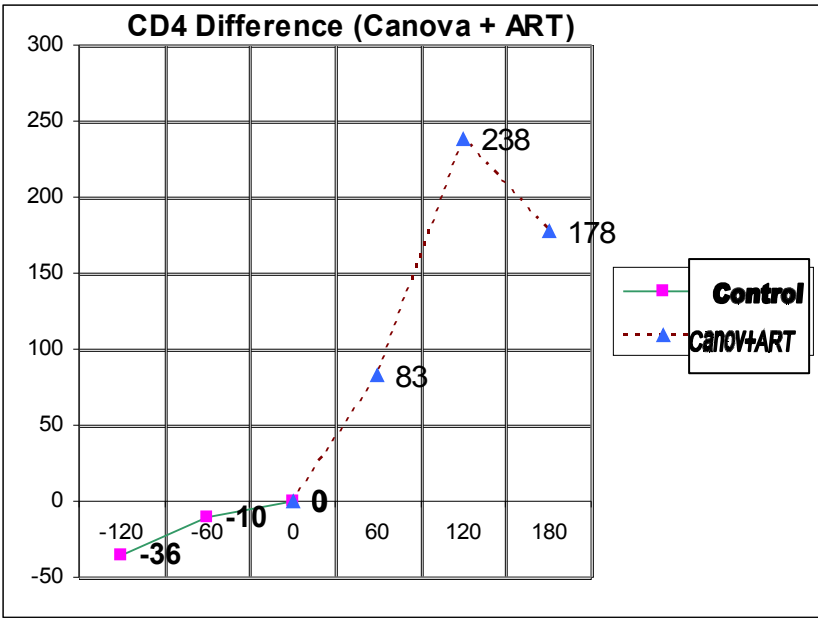
CD4 Count:

Group	Day 0	Day 60	Day 120	Day 180	Differenc	% Diff.	Comment
Canova	171	311	307	261	90	53.00%	Highly
ART+Canova	128	211	366	306	178	139%	significant

CD4 Count: Comparison with Control

Group	Day 0	Day 180	Diff.	%	Comment
Control	183	161	22	-12	
Canova	171	261	90	+53 (65)	Highly Significant
ART+ Canova	128	306	178	+139 (151)	





Viral load

Group	Day 0	Day 180	Difference	Comment
Canova	126,392	65,094	61,298	Signicant
ART+ Canova	43,983	5,78	38,194 1Log diff.	Highly significant

IMPRESSIONS:

1. The patients on Canova had a feeling of general well being through out the study period. None of them developed any Opportunistic Infection during the study period. None of them developed any demonstrable adverse event. All of them remained fully productive in their day-to-day life.

2. Follow-up was excellent (22/26 + 2 more are expected to follow-up).

3. Weight:

In almost all the patients there has been weight gain ranging from 2 to 6 kg. While in the Gr. 1, average weight gain was 3.11 kg and in Gr. 2 average weight gain was 2.76 kg . Both are statistically significant, as they are >5%.

4. Haemoglobin and Red Blood Count:

There has been no statistical significance in the pre and post-study HB% levels and RBC levels in both the groups.

5. CD4 Lymphocyte Count:

There has been a significant difference in pre and post-study CD4Lymphocytic count in patients with in Group 1 (53%), while in the Gr. 2 it was (139%) increase. Both are highly significant.

Out of 22 patients, we had one patient whose CD4 count was same at the end of six months.

One had a drop in his CD4 count, necessitating us to start ART. Strangely this patient's Viral Load at Day 0 was 218,000 and it jumped to 16,70,000 at the end of 180 days; (which is being reassessed). His CD4 count at Day-0 was 145 and it became 129 at Day 180. There must have been some concurrent illness that we couldn't diagnose due to limitation of investigation tools.

(a) There has been statistically significant change for the better in the absolute CD4 count in both the groups: an average gain of 53% in group with only Canova group; while there was a record improvement of 139% in the ART+Canova group

(b) The patients from group 1 had shown much better CD4 counts at day 60 and day 120 - 82% and 80% respectively, as compared to day 180 when it was 53%.

(c) The patients from group 2 had shown 65% improvement in CD4 count at day 60, while a record 186% at Day 120 and coming down marginally to 139% at Day 180.

d) The observation of comparatively much higher increase in CD4 counts at day 60 and day 120 and then some reduction at Day 180 prompts further follow-up and study. May be higher dose of Canova is required after initial prompting of 3-4 months. May be it will cover-up on its own, as we have seen in two of the study patients who had followed-up recently at an interval of 2 months post-study? In both of them there was upward jump in CD4 count by further 45% and 90% respectively as compared to Day 180.

Adverse Effects:

There were no demonstrable side-effects noted whatsoever with Canova. We were highly impressed with the performance of this formulation that the patients had no complaints whatsoever, except for one patient having hypersensitivity to Canova forcing us to stop the same.

One of the patient developed Herpes Zoster during the study period. It is considered a sign of good immunity, due to Immune Reconstitution Inflammatory Syndrome (IRIS) and not the adverse effect.

No Significant Change in Liver Function tests of patients.

FINAL IMPRESSIONS:

- We highly recommend CANOVA – homeopathic formulation manufactured and marked by Canova Homeopathic Pvt. Ltd., Ahmedabad as a Nutritional Supplement cum- Immunomodulator for the patients of HIV/AIDS.
- Canova had shown demonstrable/impressive increase in CD4 count and body weight
- Canova had shown decrease in HIV Viral Load from significant in ART-Naïve patients to highly significant in ART-resistant patients
- Canova had shown improvement in generalized well-being during the study among moderately immuno-compromised HIV/AIDS patients and significant increase in body weight over 6 months period.
- We found that Canova, when given alone, improves the quality of life in immuno-compromised patients; who had CD4 counts between 150 and 200.
- Similarly, Canova improves the immune-status in HIV/AIDS patients in whom the Anti-Retroviral Treatment (ART) become ineffective; which are often demonstrated by fall in absolute CD4 counts – an indicator of falling immunity, and fresh episodes of opportunistic infections despite being on ART.

1. Canova has been found efficacious in improving quality of life in patients of HIV/AIDS.
2. Canova has been found efficacious in elevating the number of CD4 count in HIV/AIDS patients by a record 53% in whom no other treatment than the Canova was given. Similarly, it has shown a record 139% increase in CD4 count of patients who were on ART, but become resistant to the same and their CD4 was constantly falling or become static.
3. Canova has been found effective in preventing the onset of Opportunistic Infections in HIV/AIDS patients.
4. Canova has shown significant decline in the plasma viral load in patients of HIV/AIDS.

Recommendations:

The formulation should be aggressively marketed as currently there is no known, low-cost and safe immunomodulator available globally, particularly which can work in ART-Naïve patients at CD4 counts levels as low as 150 to 200. The product is a ray of hope for millions of HIV infected people, most of whom can not afford the Anti- retroviral Therapy (ART).

We are aware of the limitations of our study, being a small sample size. However, we feel this sample size was good enough to establish the

- (a) Safety of the formulation
- (b) Acceptability of the formulation
- (c) Ease of taking medication, limited dosage schedule
- (d) Efficacy of the formulation

Patients developing opportunistic infections during the course of this medication should take treatment for those conditions as per the routine guidelines.

We recommend a further follow-up of the patients under study for one more year and add few more patients to the study.

The patients can be further divided into two categories each – those on-continued Canova and those without Canova. Thus there will be 4 set of patients:

- A 1 – With continued Canova only
- A 2 - No further Canova;
- B 1 – With Continued Canova + ART
- B 2 - No further Canova, Only ART

Follow-up with Laboratory tests including CD4 counts, physical check-up is recommended.

This will establish, whether the Canova should be given continuously. The formulation should be priced in such a way so as to be affordable to majority of HIV/AIDS patients.

It was pleasure working with this project and the patients were gratified. There has been a consistent demand for these formulations from the study-patients as well as those who came to know of this study.



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