



# Integrated Cancer Treatment and Research Centre Wagholi, Pune, INDIA



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# **Effectiveness of Ayurvedic treatment in alleviating side-effects of radiotherapy in oropharyngeal cancer patients and its relationship with improvement in immune status of the host**

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# Introduction

- Ayurveda, an ancient Indian system of medicine is practised even today for various illnesses especially those which are caused by reduced immune responses
- Recently combinations of Ayurvedic drugs are recommended for cancer as an adjunct therapy
- Non-toxicity of Ayurvedic drug combinations makes the drugs acceptable by patients
- Oral cancer ranks in the top three of all cancers in India with an alarming increase in younger age. High incidence is associated with use of smokeless tobacco
- The preference of treatment for oropharyngeal cancers is surgery followed by radiotherapy and / or chemotherapy depending upon grade and stage of disease

# Introduction

- Side effects of Radiotherapy often affect immune system and compromise quality of life of cancer patient
- Side effects are also reflected in Quality of life as the treatment hampers intake of food
- This major concern is being addressed worldwide
- We have used selected Ayurvedic medicines, known to act on pathological conditions similar to side-effects of radiotherapy, as per Ayurvedic texts
- In the first part of this study we have clinically assessed the efficacy of Ayurvedic drugs in alleviating side effects of radiotherapy
- In the second part, we have assessed the possible improvement in immune status of these patients

# Patient population

**Inclusion criteria:** Patients with cancers of all sites in oropharynx, patients of all stages and grades eligible for radiation therapy  
All patients had undergone surgery before radiation

**Exclusion criteria:** Oral cavity cancer patients who have received palliative radiotherapy, curative chemotherapy along with radiotherapy and those who have undergone Radiotherapy in the past

**Treatment:** Patients received radiation dose up to 6600 cGy in 30-35 fractions in 5-6 weeks

**First part of the study:**

**Group 1:** 35 patients treated with radiotherapy alone

**Group 2:** 35 patients who received combinations of Ayurvedic drugs from the beginning of radiotherapy and continued for 3 months after radiotherapy

# Ayurvedic medication for group 2

## Ayurvedic medication –

- **Mauktikyukta Kamadudha - 250 mg with milk twice a day**
- **Mauktikyukta Praval Panchamrut - 250 mg with milk twice a day**
- **Ananta Vati - 1 gm with water after both meals**
- **Yashtimadhu Ghruta - 5 gm before both meals**
- **Yashtimadhu Ghrut - local application in the mouth**

# Assessment criteria for group 1 and 2

1) Common Toxicity Criteria (CTC, Designed by NIH/NCI) related to symptoms associated with oral cancers : Stomatitis , Trismus, Dysphagia, Xerostomia, Nausea, Excessive salivation and Weight loss

- These symptoms were assessed at the end of radiotherapy and 3 months after radiotherapy
- Symptoms are grades as 0 (No symptom) to 4 (Severe symptom) as per CTC

2) Karnofsky score

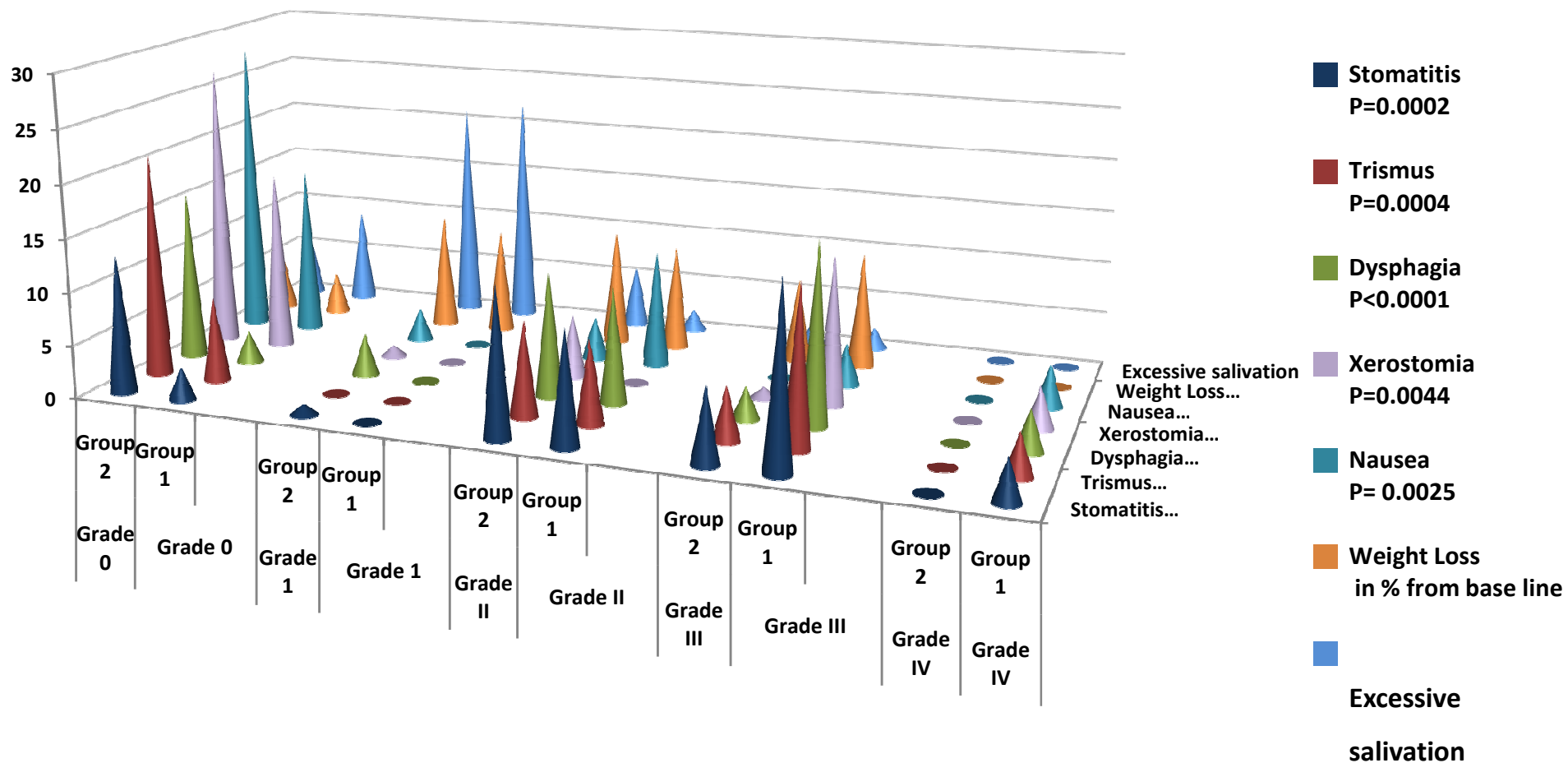
3) QLQ C30 (EORTC – European Organization of Research and Treatment in Cancer) – Quality of Life Questionnaire - Functional, symptom and global score [the later indicating general well-being]

Criteria 2 and 3 were assessed before and after radiation

All the criteria are internationally accepted outcome measures to assess side-effects and Quality of Life of cancer patients under treatment

# Results - symptoms

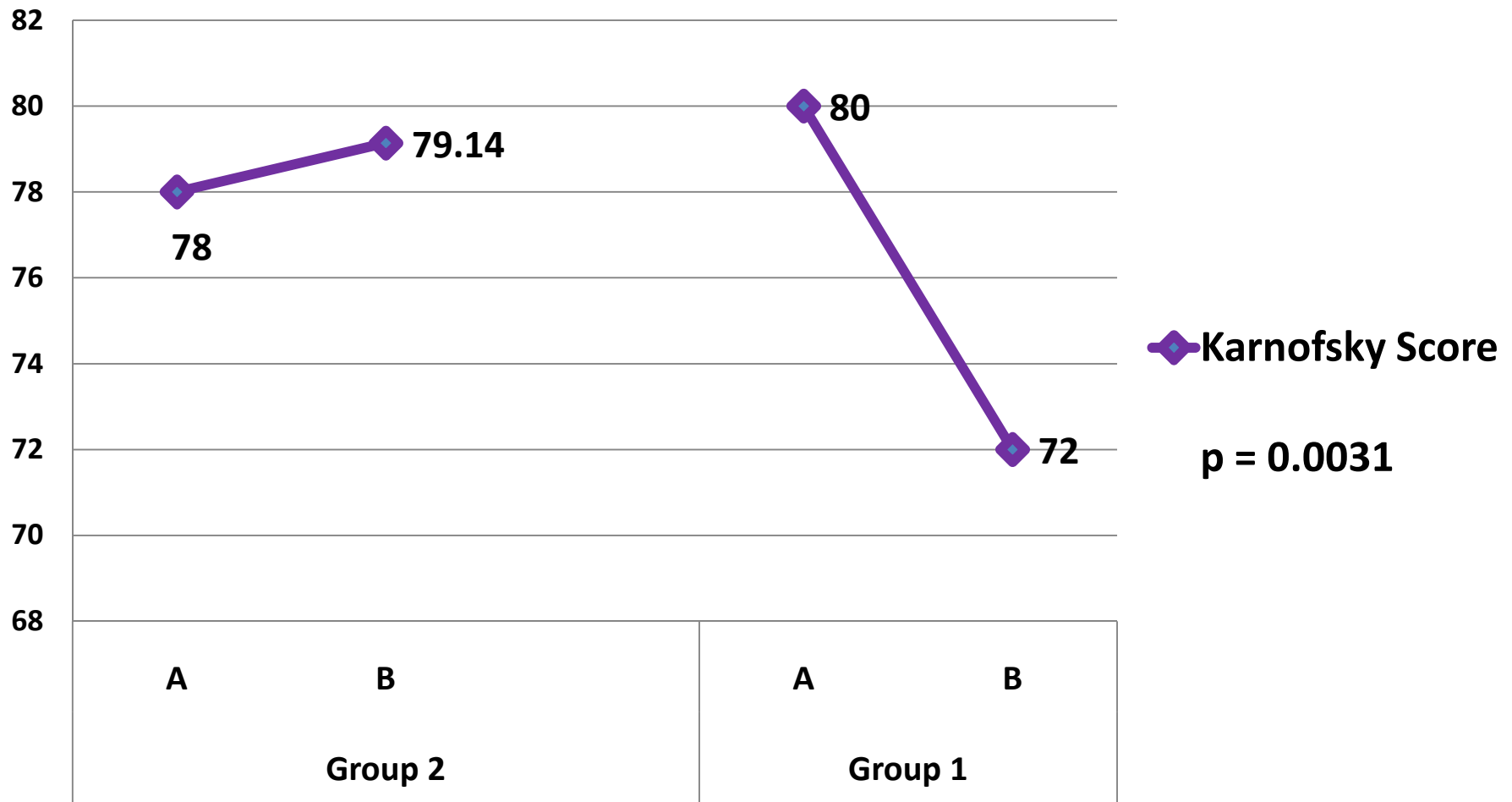
## Graphical representation of mean values depicting side effects of radiotherapy





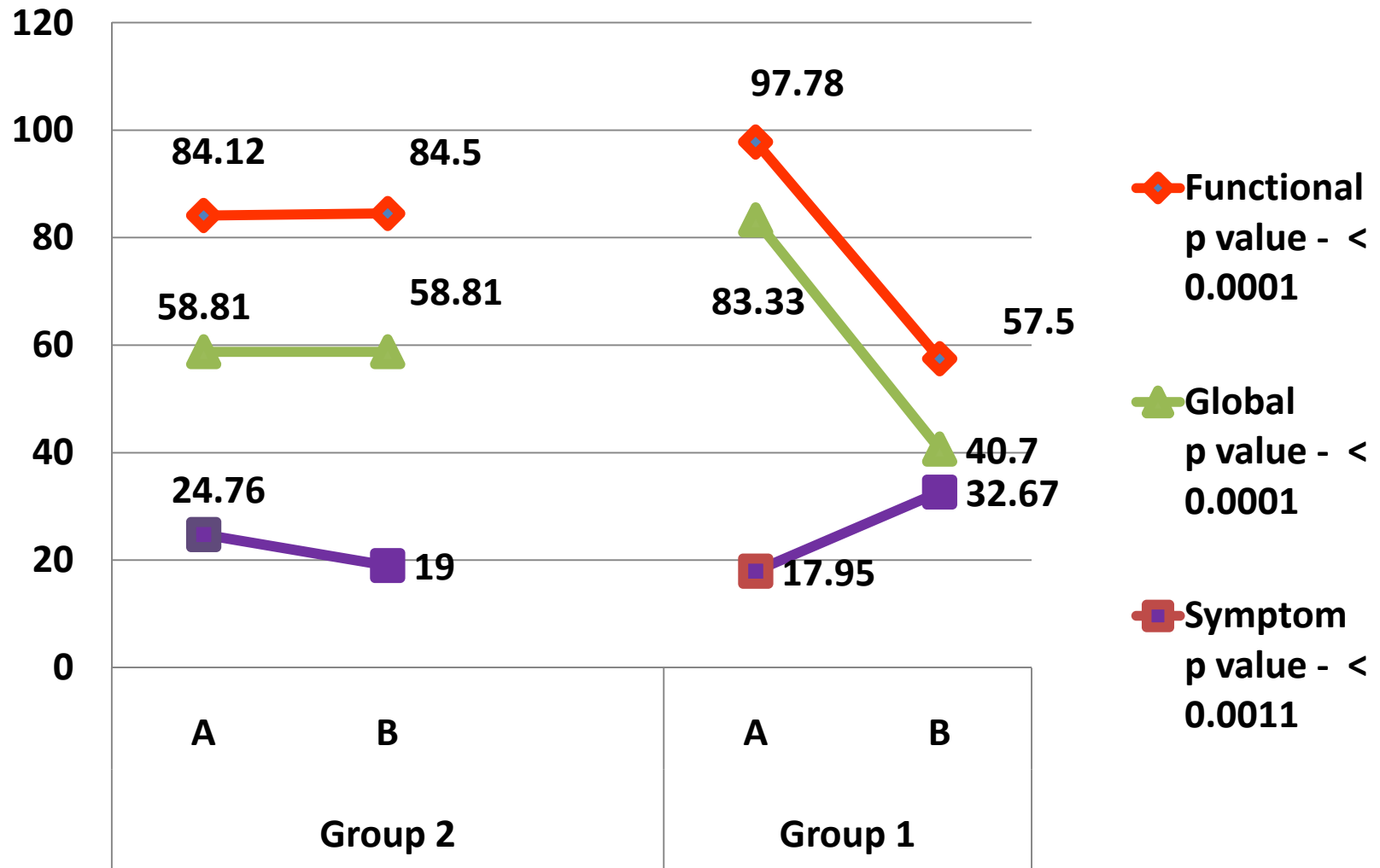
**Graphical representation of mean values (35 samples)  
depicting Karnofsky score**

**A – Before Radiotherapy , B – After Radiotherapy**



## Graphical representation of mean values depicting functional, symptom and global score of QLQ

A – Before Radiotherapy , B – After Radiotherapy



# Conclusion

- 1. Ayurvedic treatment is effective in management of Radiotherapy side-effects in oral cavity cancer patients such as stomatitis, trismus, dysphagia, xerostomia and nausea**
- 2. Karnofsky score representing ability to conduct daily activities, as judged by clinician, improved significantly with adjunct Ayurvedic treatment**
- 3. Global score of QLQ indicative of general feeling of wellbeing, as assessed by patient was significantly reduced in group 1 patients while in group 2 patients the feeling of well being did not worsen as reported by the patients themselves**

## Part 2

# Effect of Ayurvedic medicines on immune response of Oral Squamous cell carcinoma (OSCC) patients: preliminary studies.

Relationship of oral Ayurvedic medicines (OAM) used in this study with immune response -

a) Rasayana: 4 drugs categorised as Rasayana are used in this study. They are known to boost up immunity as per Ayurvedic texts

b) Two drugs used in this study are known to reduce inflammatory responses

c) Selective Panchakarma procedures used for side-effects in OSCC include medicated oil treatments, local applications in mouth region and massage meant for systemic and local detoxification.

This treatment was given to a group of patients treated with RT and OAM, who continued to show side effects 1 to 6 months post RT

# Immunological criteria assessed

- 1) Immunophenotyping - Total T & B cells and T cells subsets in PBMC and mitogen induced proliferation of T and B cells
- 2) Markers of tumor load: CD105 and Ki67
- 3) Assessment of cytokines carried out in saliva and serum, local responses were indicated by salivary samples, therefore data presented will be on salivary samples
  - Type 1 cytokines: IFN- $\gamma$  and TNF- $\alpha$
  - Type 2 cytokines: IL-1  $\beta$ , IL-6, IL-8 and IL-10, indicative of inflammatory status
- 4) Immune complexes and IgA in saliva indicative of local immune response.

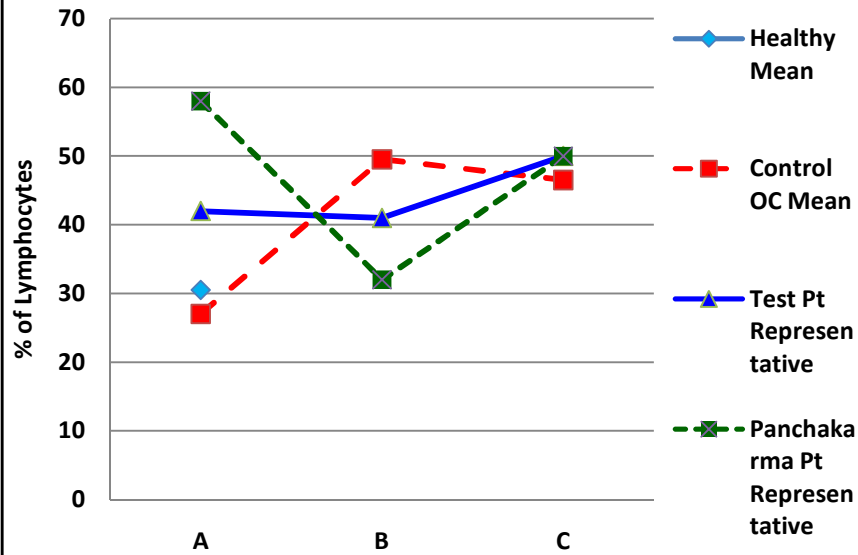
# Grouping of patients

- Major limitation of the study:

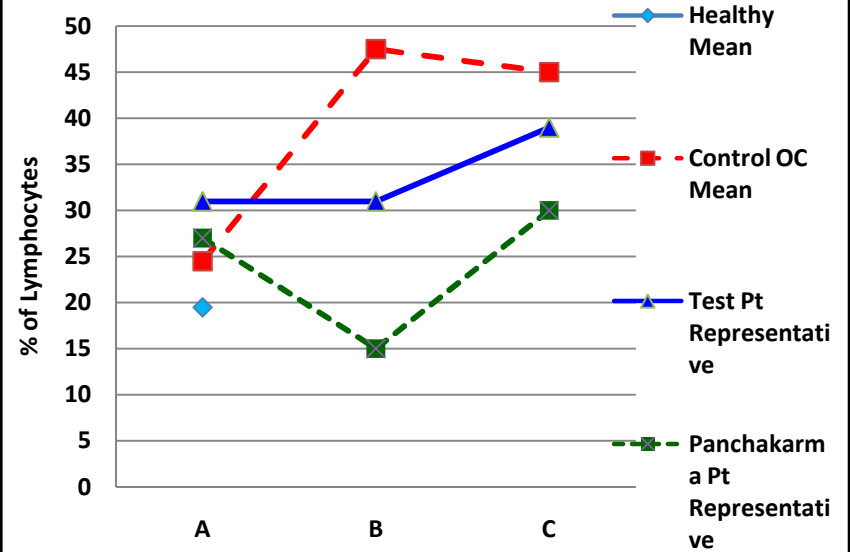
## 1. small sample size.

- Group 1a – controls: 1 normal healthy donor,  
1 chewer with mild leukoplakia  
1 chewer with severe leukoplakia
  - Group 1b – OSCC patients treated with RT alone – 2
  - Group 2a – OSCC patients treated with RT and OAM – 5
  - Group 2b – OSCC patients treated with RT + OAM + Panchakarma -6
- ## 2. Large variation in test results in individual samples in 2a and 2b, statistical analysis was therefore not conclusive although pattern of response was same
- Time point of assessment 2a: A - beginning of RT + OAM, B – at the end of RT + OAM, C – 1 month post RT + OAM  
2b: A – beginning of Panchakarma (OAM continued), B – at the end of Panchakarma (OAM continued), C – 1 month post Panchakarma (OAM continued)

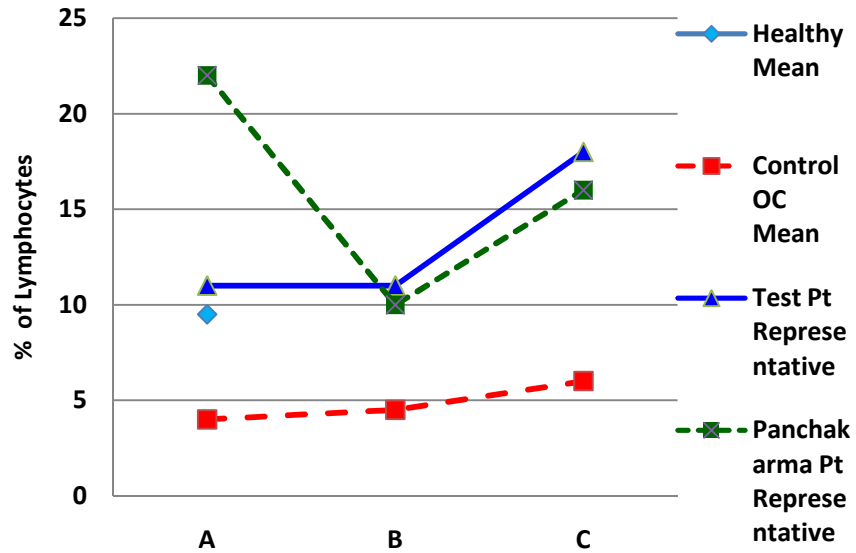
### Total CD 3 in PBMC



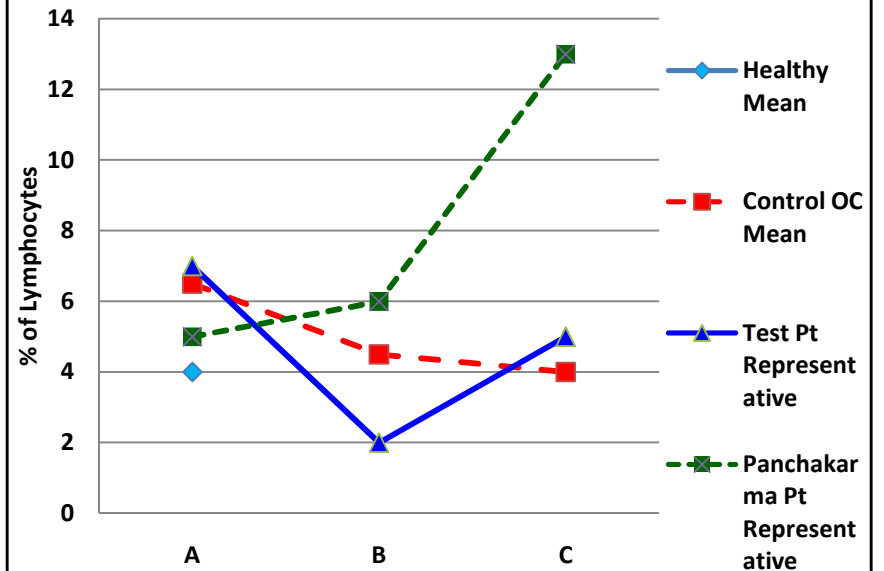
### Total CD 4 in PBMC

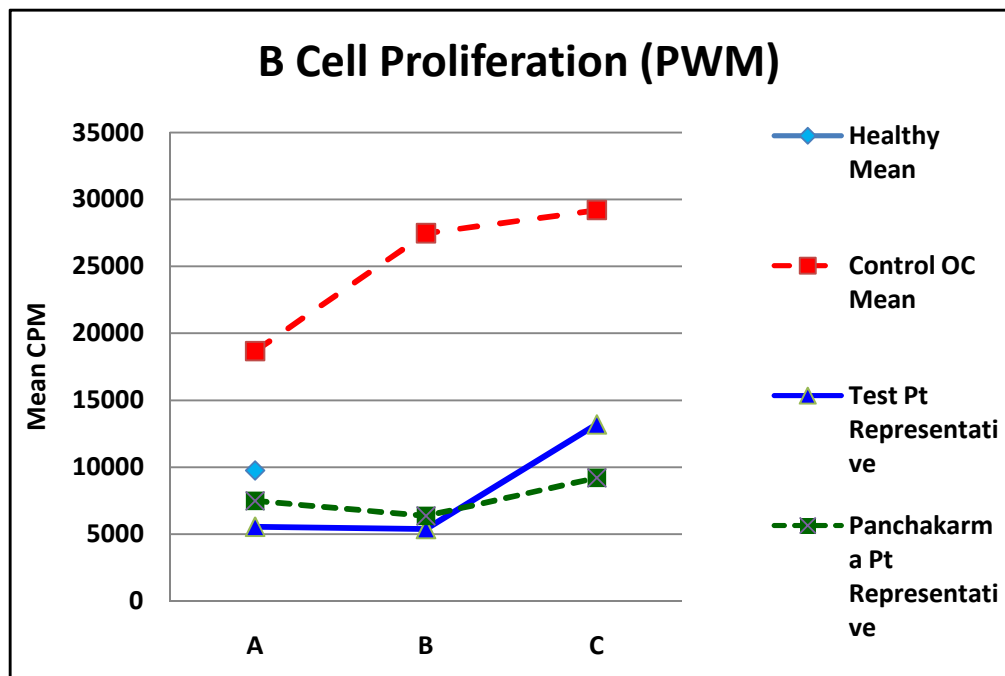
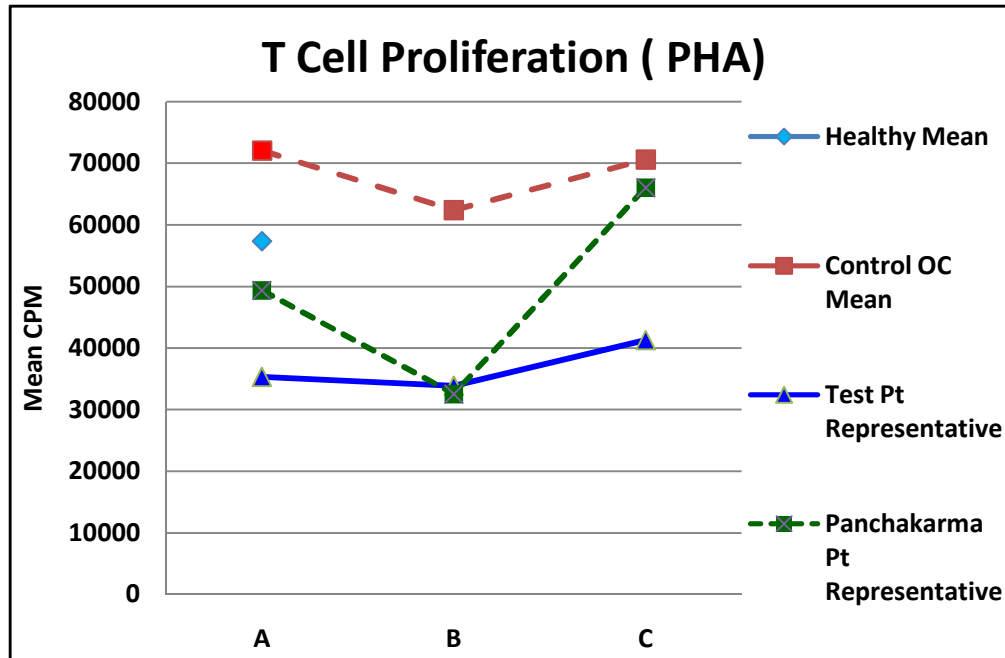


### Total CD 8 in PBMC



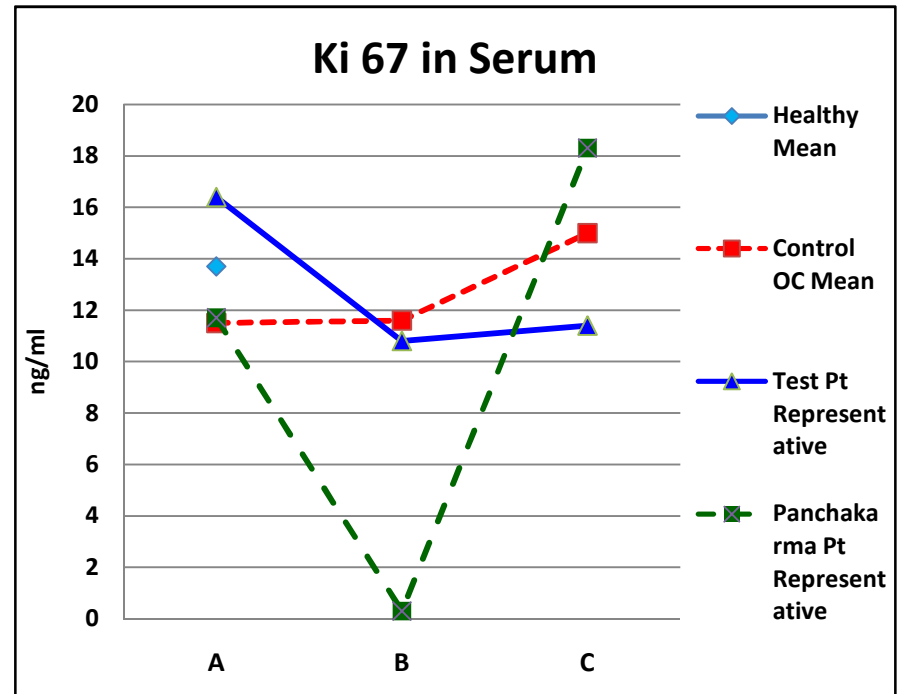
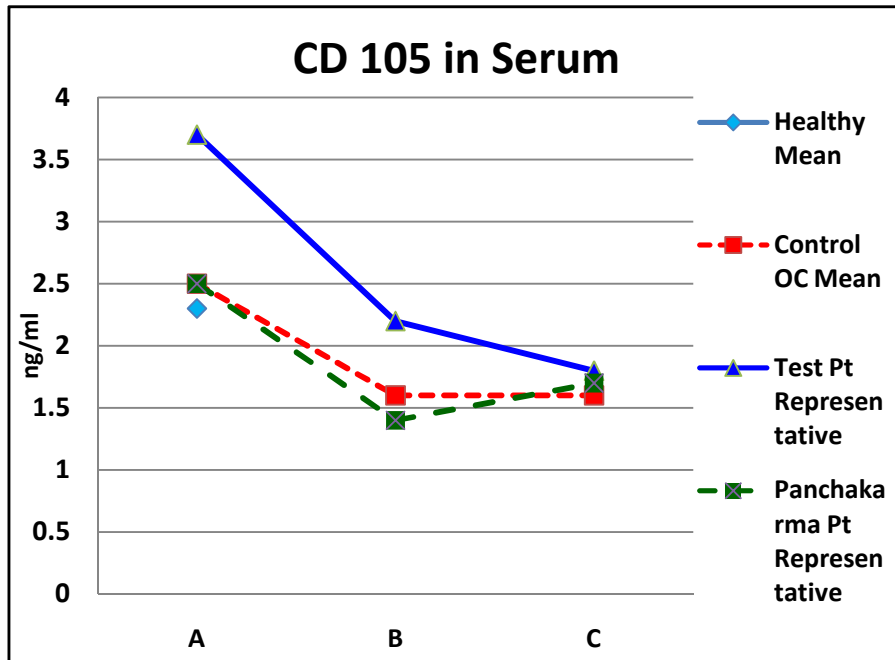
### Total CD 19 in PBMC



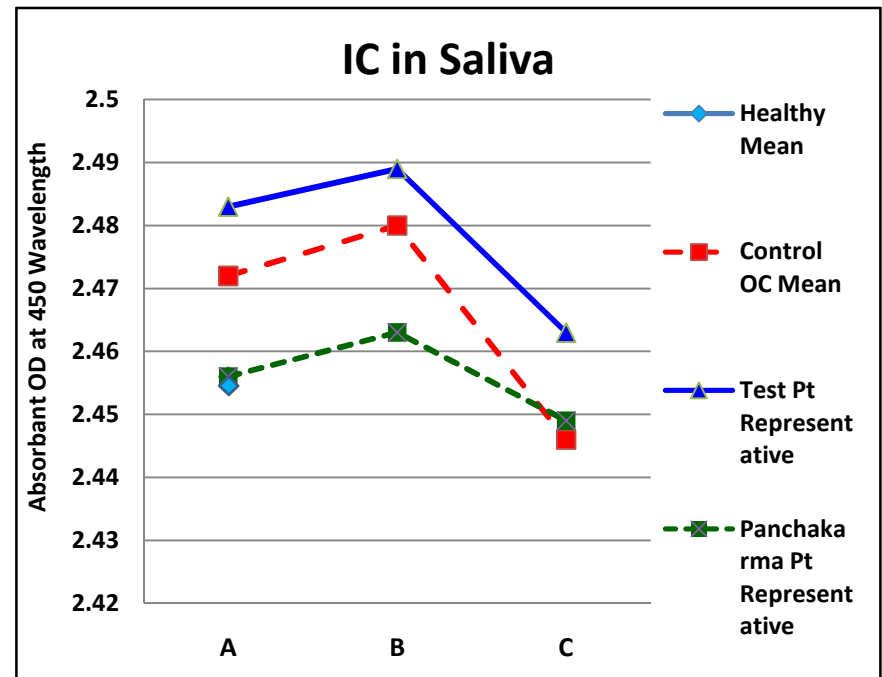
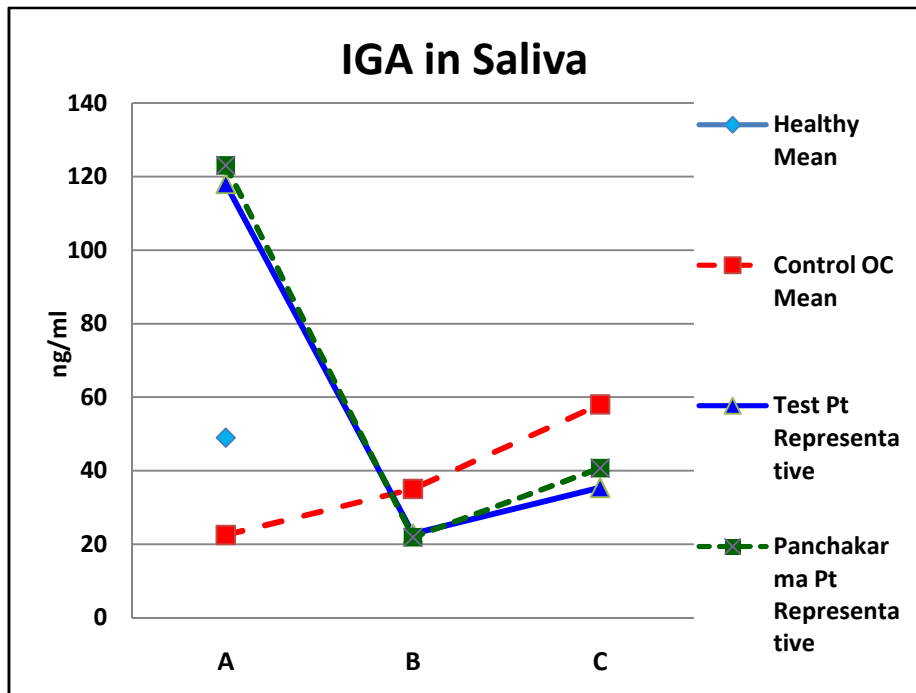




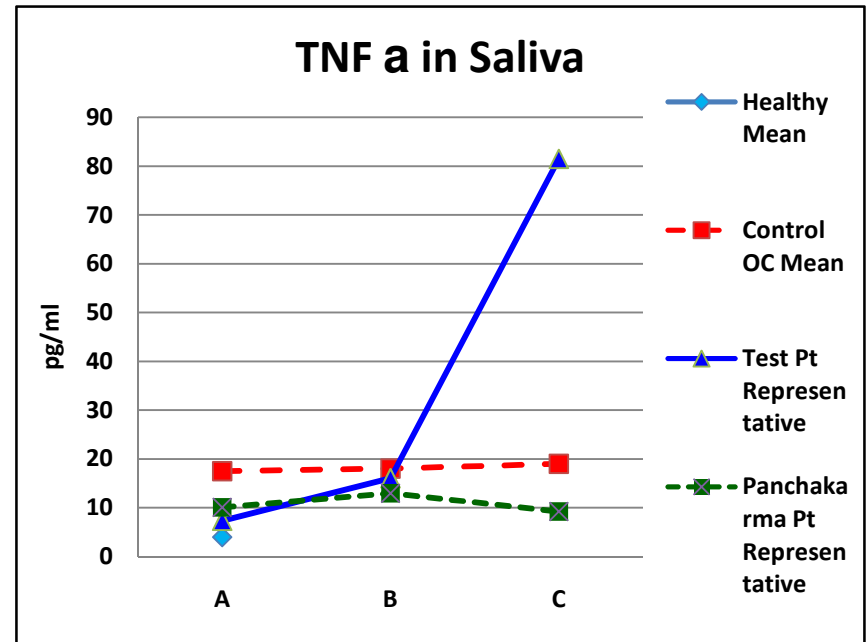
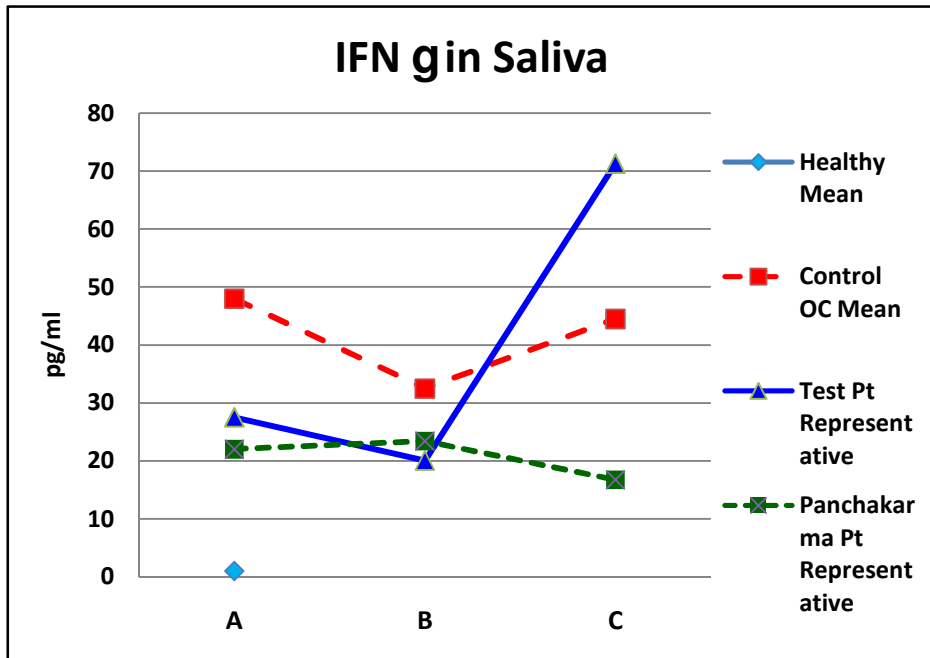
# Tumor markers



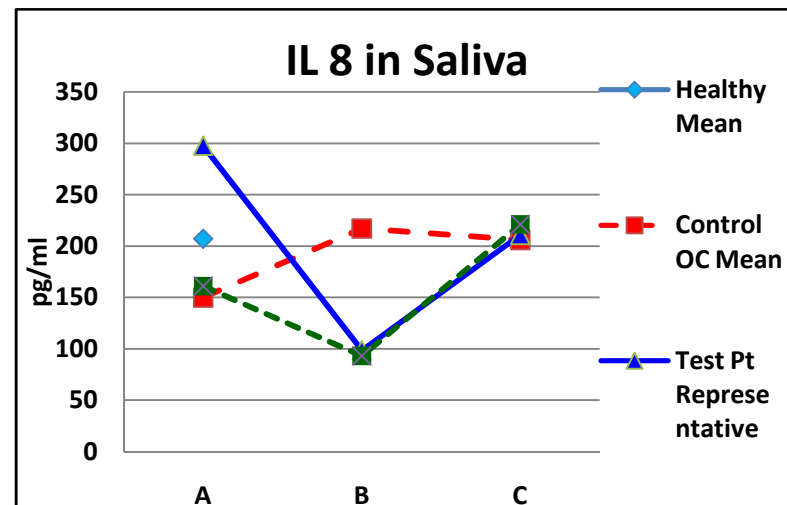
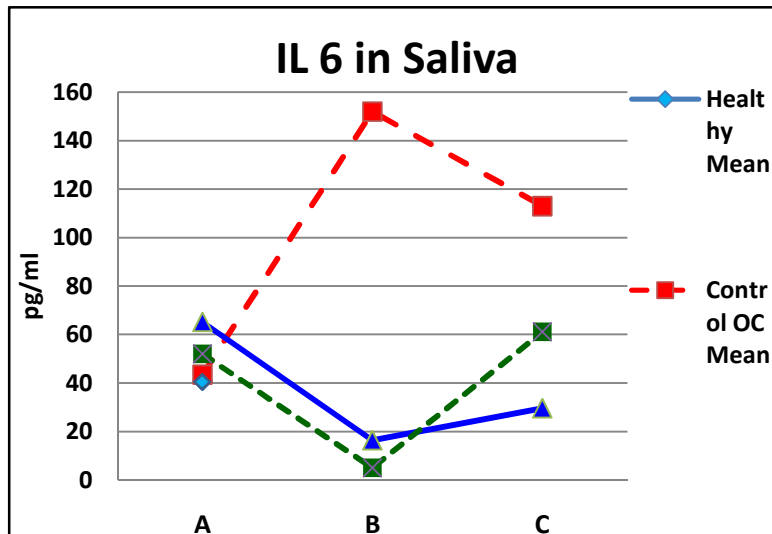
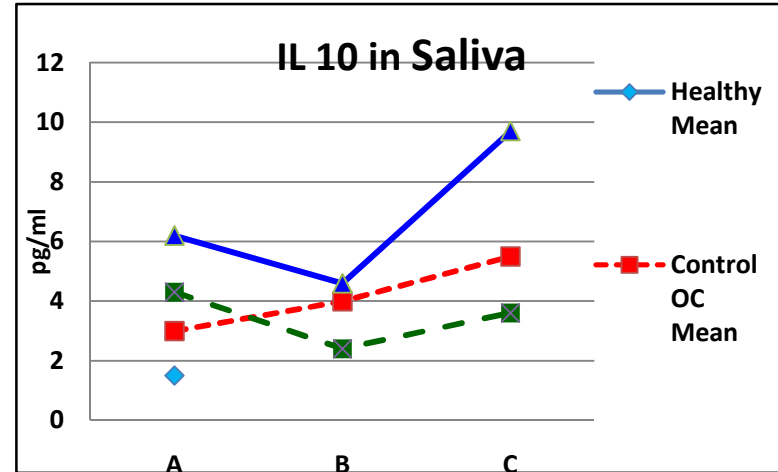
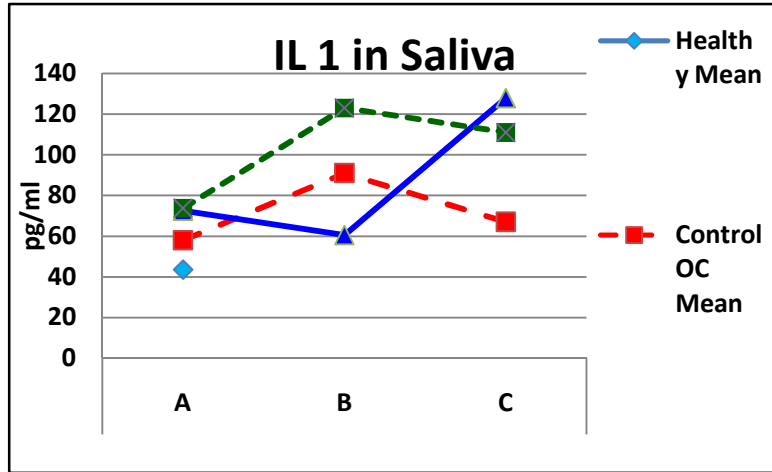
# Local immune response



# Type 1 cytokines in saliva



# Type 2 cytokines in saliva



# Tentative conclusion

Based on the preliminary data, the trends indicate-

- 1) Local immune response in saliva shows better association with treatment outcome
- 2) Immune recovery in the form of a) phenotypes in peripheral blood b) proliferative responses in T and B cells c) oral mucosal immunity d) type 1 cytokines e) reduction in circulating tumour markers is seen in patients treated with oral administration of Ayurvedic drugs along with RT.
- 3) The pro inflammatory cytokines showed decrease after radiation. In both 2a and 2b patients this response appears to be related to Ayurvedic treatment
- 4) Type 1 cytokines IFN- $\gamma$  and TNF- $\alpha$  show low levels initially which are increased in both 2a and 2b after 1 month of radiotherapy, which is perhaps indicative of polarization towards TH<sub>1</sub> response

**Further research leads require inclusion of larger cohort and extended follow-up with OAM to confirm the findings**



# Controls and TNM classification

<b>1) 4 parameters compared in 3 normal donors</b>				
<b>Name of Group</b>	<b>Proliferation T cell</b>	<b>CD3</b>	<b>IL 10 in Saliva</b>	<b>CD 105 in Saliva</b>
<b>Healthy</b>	<b>65187</b>	<b>35</b>	<b>4.3</b>	<b>1.8</b>
<b>Tobacco chewer with mild leukoplakia</b>	<b>33506</b>	<b>29</b>	<b>0.9</b>	<b>3.2</b>
<b>Tobacco chewer with severe leukoplakia</b>	<b>73356</b>	<b>27</b>	<b>1.4</b>	<b>2.1</b>
<b>Mean - Healthy</b>	<b>57350</b>	<b>33</b>	<b>2.2</b>	<b>2.4</b>
<b>2) Responses of T1/T2 Vs T3/T4 patients</b>				
<b>Stage</b>	<b>Mean values</b>			
<b>Stage I + II</b>	<b>65437</b>	<b>41</b>	<b>2.6</b>	<b>2.5</b>
<b>Stage III + IV</b>	<b>54132</b>	<b>53.8</b>	<b>5.1</b>	<b>2.62</b>