Oral Abstract Session II
Friday, 04/13/2018, 3:00-5:00pm

= Oral Abstract Number, *Presenter

To conserve space, we list only the institution and the country submitted as 1st organization.

Abstracts Committee:
Chair: Kentaro Ikeda, DDS, MPH
Co-Chair: Bhavik Desai, DMD, PhD

The Parotid Gland in Primary Sjögren's Syndrome: Association of Ultrasound, Histopathology and Saliva Production in the Diagnostic Work-up

*Konstantina Delli, Esther Mossel, Erlin Haacke, Bert van der Vegt, Suzanne Arends, Uzma Nakshbandi, Jolien F van Nimwegen, Alja J Stel, Fred KL Spijkervet, Frans GM Kroese, Arjan Vissink, Hendrika Bootsma
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Objectives:

The parotid glands are commonly involved in primary Sjögren's syndrome (pSS). The aim of this study was to assess the diagnostic accuracy of ultrasound of the parotid glands (PSGUS) compared with the parotid histopathology and parotid saliva production.

Methods:

We included consecutive patients suspected with pSS. All patients underwent a full diagnostic work-up according to ACR-EULAR criteria, including PSGUS, parotid gland biopsy and collection of stimulated parotid saliva. For PSGUS, the average score of hypoechogenic areas in both parotid glands was applied (range 0-3). On H&E stained sections from parotid gland biopsies, focus score, presence of lymphoepithelial lesions (LELs) and germinal centers (GCs) were assessed. The area of lymphocytic infiltrate was calculated digitally on CD45 stained sections. The relative increase of IgG expressing plasma cells ($\geq$30%) was evaluated on sections stained for IgA and IgG. PSGUS score was associated with focus score, percentage of infiltrate and saliva flow and compared with plasma cell shift, LELs and GCs by calculating the percentage of absolute agreement, sensitivity and specificity.

Results:

In total, of the 111 included patients, 53 fulfilled the ACR-EULAR classification criteria for pSS. PSGUS score showed moderate correlation with focus score (ρ=0.494, p<0.001) and percentage of lymphocytic infiltrate (ρ=0.575, p<0.001). There was a moderate to good absolute agreement between PSGUS and focus score (78.5%), plasma cell shift (79.8%), LELs (81.4%) and GCs (82.7%). 'Presence of hypoechogenic areas' was not very sensitive to predict focus score (69.2%), plasma cell shift (45.8%), LELs (61.5%) or GCs (34.6%). Interestingly, almost all patients with <25% presence of hypoechogenic areas in glandular parenchyma were also negative for GCs (98.7%). A substantial amount of these patients did not have a positive focus score (81.4%), plasma cell shift (90.7%) or LELs (87.8%). There was a fair reversed correlation between PSGUS and stimulated parotid saliva flow (ρ=-0.259, p=0.07).

Conclusions:

This is the first study comparing the diagnostic accuracy of PSGUS with histopathology and salivary secretion in detail. PSGUS and histopathology are stronger associated than PSGUS and parotid secretion. Specificity of PSGUS increases when results are compared to plasma cell shift, LELs and GCs, instead of focus score.

Novel Anti-CD40 Monoclonal Antibody CFZ533 in Patients with Primary Sjogren Syndrome: A Phase IIa Double-Blind, Placebo–Controlled Randomized Trial

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Objectives:

Primary Sjogren syndrome (pSS) is a progressive autoimmune disease characterized by formation of ectopic germinal centers in exocrine glands and secretory gland dysfunction with subset of patients developing extraglandular manifestations. CFZ533 is a novel monoclonal antibody that selectively blocks CD40, a co-stimulatory pathway receptor essential for germinal center reactions and other immune-mediated functions implicated in pSS pathogenesis. We conducted a randomized, double–blind, placebo-controlled, multi-centric, partial cross-over Phase IIa Proof of Concept (PoC) study to evaluate the safety, tolerability and efficacy of CFZ533 in patients with pSS.

Methods:

Clinically active (EULAR Sjögren's Syndrome Disease Activity Index [ESSDAI]≥6) pSS patients were randomized to receive four s.c. doses of 3 mg/kg.CFZ533 or placebo (2:1, Cohort 1) or 10mg/kg i.v. CFZ533 or placebo (2:1, Cohort 2) over 12 weeks (Period 1). Four additional doses of 3mg/kg s.c. or 10mg/kg i.v. CFZ533, respectively, were administered in an open-label extension (Period 2) for 12 weeks. Key outcomes included safety and efficacy (defined as reduction in ESSDAI) after 12 weeks of treatment. Patient reported outcomes included EULAR Sjögren Syndrome Patient Reported Index (ESSPRI), Multi-dimensional Fatigue Inventory (MFI), Patient's Global Assessment, SF-36. Physician's Global Assessment was also monitored.

Results:

Forty-four patients were enrolled: 8 patients received 3mg/kg s.c. CFZ533 and 4 placebo in Cohort 1 and 21 received 10mg/kg i.v. CFZ533 and 11 placebo in Cohort 2. Overall, CFZ533 was safe and well tolerated, and the majority of AEs were mild or moderate. There was a single SAE (bacterial conjunctivitis) in the 3mg/kg s.c. cohort and one SAE (atrial fibrillation) in the 10mg/kg i.v. cohort, both of which were unrelated to the study drug. While no efficacy was observed in Cohort 1, improvements in ESSPRI, MFI, and Patient's Global Assessment were observed. Physician`s Global Assessment showed statistically significant improvement. In cohort 2, efficacy, based on mean reduction of ESSDAI, was statistically and clinically significant after 12 weeks of treatment compared to placebo [-5.64 (95%CI=1.02,–10.58)]. Physician`s Global Assessment also showed statistical significance [-13.72 (95%CI=23.41, -4.04)]

Conclusion:

Testing a blocking, non-depleting anti-CD40 antibody for the first time in pSS, suggests that CFZ533 may offer a safe/efficacious new treatment modality.

Novel Bilayer Mucoadhesive Patches for Delivery of Clobetasol-17-Propionate to the Oral Mucosa to Treat Oral Lichen Planus; An in vitro and in vivo Evaluation

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Objectives:

Oral lichen planus (OLP) and recurrent aphthous stomatitis (RAS) are chronic inflammatory conditions often characterised by erosive and/or painful oral lesions that have a considerable impact on quality of life. Current treatment often necessitates the use of steroids in the form of mouthwashes, creams or ointments but these are often ineffective due to inadequate drug contact times with the lesion. Here we evaluate the performance of novel bilayer mucoadhesive patches for uni-directional delivery of the steroid Clobetasol-17-propionate to the oral mucosa.

Methods:

Electrospun polymeric patches with an impermeable backing layer and mucoadhesive drug delivery layer were produced and characterised for their physical properties in the laboratory. The drug release profile, drug penetration and cytotoxicity of the system in delivering Clobetasol-17-proprionate was evaluated using ex-vivo porcine oral mucosa and tissue engineered human oral mucosa. The ability of the system to deliver Clobetasol -17-proprionate effectively into the oral mucosa, and local and systemic drug safety was then confirmed in in vivo mini-pig studies before evaluation of residence time and acceptability of the drug delivery system in a human volunteer study.

Results:

Clobetasol-17-propionate incorporated into the patches was released in a sustained manner in both tissue-engineered oral mucosa and ex vivo porcine mucosa. Clobetasol-17 propionate-loaded patches were further evaluated for residence time and drug release in an in vivo animal model and demonstrated prolonged adhesion and drug release at therapeutic-relevant doses and time points without local or systemic toxicity. Human studies confirmed long adhesion (residence) times and high levels of patient acceptability for use of the oral adhesive patches for treatment of oral mucosal disease.

Conclusions:

These data show that electrospun patches are adherent to mucosal tissue without causing tissue damage, and can successfully be loaded with and release Clobetasol and potentially other clinically active drugs into the oral mucosae in a sustained therapeutic manner. These patches hold great promise for improving the treatment of OLP, RAS and other immunoinflammatory oral diseases and are ready to enter phase 2 clinical trials.

The Rivelin® Patch – A New Treatment Strategy for Oral Lichen Planus (OLP)

Thomas Ruzicka, Marlene Seegräber, Thomas Bieber, Bernhard Homey, *<u>Richeal Ni Riordain</u>, Lars Siim Madsen, Jens Hansen
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Objectives:

Investigate adhesion time and tolerability of plain patches when applied to symptomatic OLP lesions, as well as evaluating the feasibility to apply plain patches in the oral cavity.

Methods:

A total of 13 symptomatic OLP were enrolled in this open label, single arm study, where 12 out of 13 OLP patients completed the study. A target lesion was identified by the investigator during enrolment and subjects applied 1-2 patches to the target lesion twice daily for 28 days. Patients were assessed at weekly visits and data on adhesion time and symptoms were collected in daily diaries.

Results:

The likelihood of an adhesion time longer than the pre-specified 15 minutes was >90% (mean adhesion time was ~ 90 mins). A questionnaire assessment of the tolerability and sensation of the Rivelin plain patches revealed a profound positive feedback on the patches. No worsening of symptoms (COMDQ) and lesions (Guy´s DAS) were observed at the target lesions when applying patches twice daily for 28 days, in fact pain scores at application and removal of the patches were lower than the general pain. All subjects could successful apply patches.

Conclusions:

The Rivelin® patch provide a new unique treatment strategy. Based on these findings the Clo patch will be evaluated in a phase 2b study in symptomatic OLP patients with the assumption of providing longer contact time of Clobetasol at lesion site (adhesion time at 90 mins), securing a unidirectional fixed dosing (two-layer patch) and a high compliance is expected (all patients could apply patches with a favorable tolerability and sensation profile).

#15 – 3:40-3:50pm
Implications of Oral GVHD Diagnosed Clinically Between Days 70 -100 post Allogeneic Hematopoietic Cell Transplantation in the Future Development of Chronic GVHD
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University of Washington, USA

Objectives:

The objective of this study was to examine the association between oral mucosal GVHD at the time of departure evaluation in individuals who were otherwise GVHD-naïve at the time of departure and the development of future chronic GVHD requiring treatment with systemic immunosuppression.

Methods:

The electronic medical records of six hundred and forty-two consecutive adults ($\geq$ 21 years of age) who received their first allogeneic HCT at Seattle Cancer Care Alliance (Seattle, WA, USA) between January 1, 2010 - June 30, 2014 were reviewed for inclusion criteria in the study.

Clinical records from Oral Medicine departure examinations were evaluated to determine oral GVHD status between Day +70-120 post-HCT. Demographic data, transplant protocols, and event timeline information were obtained from the Fred Hutchison Cancer Center (FHCRC) optical web library and the Gateway database.

Post-transplant chronic GVHD outcome data which were utilized to establish time of diagnosis and the extent of chronic GVHD involvement were obtained from the FHCRC optical web library and Gateway databases. The diagnosis of chronic GVHD was based on the 2005 NIH consensus criteria1.

Univariate and multivariable logistic regression were used to examine the association between diagnosis of oral mucosal GVHD at departure and future development of chronic GVHD in other organ systems. All analyses were performed using SAS (Statistical Analysis Software) v9.4.

Results:

Five hundred and thirty-eight patients met the criteria for inclusion in the study. In the univariate analysis, those with oral mucosal GVHD at departure were 1.5 times as likely to develop chronic GVHD when compared to those without oral GVHD at departure (OR = 1.5; 95% CI 1.1-2.2, p=0.02). A similar association was obtained in the multivariate analysis after adjusting for known risk factors for the development of chronic GVHD (OR=1.6, 95% CI 1.2-2.4, p=0.01).

Conclusions:

A clinical diagnosis of oral mucosal GVHD at the time of departure was found to be associated with increased risk for subsequent development of systemic chronic GVHD.

Individuals diagnosed with oral GVHD near Day-100 post-HCT should be trained in the recognition of the systemic signs and symptoms of emerging chronic GVHD.

Prevalence of Temporomandibular Disorder in Patients with Primary Sjögren's Syndrome

*Vishawdeep S. Dhaliwal, Davied Sanchez, Nigel Rozario, Michael T. Brennan, Joel J. Napenas
Carolinas Healthcare System, USA

Objectives:

The primary aim of this study was to determine the prevalence of temporomandibular disorder (TMD) in patients classified with primary Sjogren's syndrome (pSS) and determine risk factors for TMD in this cohort of patients.

Methods:

This was a single center, retrospective, observational study. We screened patient records of those who presented to our oral medicine clinic between March 2010 to December 2016 with oral and ocular symptoms of Sjogren's syndrome. Patients who were classified with pSS using the current classification criteria established by the American College of Rheumatology/European League Against Rheumatism(ACR-EULAR) were included. Patients with a diagnosis of TMD and had tenderness to palpation (TTP) to the TMJ and/or muscles of mastication and/or neck muscles during clinical examination were included.

Results:

145 patients met enrollment criteria, with 128 (88.8%) females. At the initial visit, a diagnosis of TMD was present in 66 (43.4%) pSS patients. Of all pSS patients 55 (37.9%) had TTP on muscles of mastication, 39 (26.9%) had TTP on neck muscles and 12 (8.3%) had TTP of the TMJ. A univariate analysis was completed for pSS patients with TMD (TMD group) vs pSS without TMD (no-TMD group). In the TMD group, 32 (50.8%) reported neurologic symptoms vs. 24(30.0%) in the no-TMD group (p=0.01). In the TMD group, 14 (22%) had fibromyalgia vs. 6(7.3%) in the no-TMD group (p=0.01). Mean age ± SD in the TMD group, 55.83 yrs ± 12.30 vs. 59.10 yrs ± 12.08 in the no-TMD group (p=0.11). We identified 5 variables by univariate analysis to include in the logistic regression analysis with the outcome of TMD vs no TMD: Sex, age, neurological symptoms, fibromyalgia and stimulated salivary flow. Using backward elimination, sex, age and stimulated salivary flow were removed from this model and the presence of fibromyalgia (odds ratio (95% CI) = 4.4 (1.4-13.2)) and neurologic complaints= 2.3 (1.1-4.7) were associated with the presence of TMD symptoms in pSS patients.

Conclusions:

Patients with pSS have a 43% prevalence of TMDs. Additionally, patients presenting with fibromyalgia are 4.4. times more likely and with neurologic complaints 2.3 times more likely to have TMD symptoms.

Referred Pain in Temporomandibular Disorders: Prevalence, Associated Factors and Effects on TMD Prognosis

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Objectives:

To describe the prevalence and clinical characteristics of pain referral in patients diagnosed with painful TMD enrolled in the RDC/TMD Validation and TMD Impact Studies. A second objective was to identify factors associated with the presence and persistence of referred pain, including Symptom Check List-90 (SCL-90) scores, number of bodily pain sites, Graded Chronic Pain Scale (GCPS). A third objective was to assess the impact of referred pain on course and prognosis of TMD. If referred pain is a phenomenon of central sensitization, then it should be associated with the presence of other signs such as elevated somatization, anxiety and depression scores.

Methods:

Data sets from the TMD Validation and Impact studies were analyzed. Referring pain sites were grouped into: extraoral (temporalis, masseter, mandibular), intraoral, and joint sites. Statistical analysis included: Frequency of referred pain, association of referred pain and persistence of referred pain with different factors, and association of referred pain with prognosis of TMD.

Results:

The rate of subjects having referred pain in the Validation study was 26.4% (162/614); 20.8% extra-oral (9.6% temporalis, 14.3% masseter, 8.6% mandibular) 10.4% intra-oral and 7.5% joint sites. Prevalence in the Impact study was 36.4% (104/286); 31.8% extra-oral (21.7% temporalis, 22.4% masseter, 9.8% mandibular), 8.0% intra-oral and 19.6% joint sites.

Conclusions:

The presence of pain referral from non-muscle sites suggests that referral cannot be explained purely by the traditionally reported peripheral presence of taut bands in muscles. These findings suggest either central mechanisms or more complex peripheral mechanisms that cannot be explained by dysfunction within muscles alone. Further analysis to correlate with other biopsychosocial factors and pain chronicity measures will provide additional insight.

Fanconi Anemia and the Oral Mucosa

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Objectives:

Patients with Fanconi anemia (FA) have an overall increased risk of 500-700 fold for head and neck squamous cell carcinoma (HNSCC) compared to the general population. Understanding the clinical course of oral mucosal changes in patients with FA is essential. The objectives of this study is to: (1) Determine the prevalence and onset of oral mucosal changes in FA patients and to; (2) Elucidate the nature and implications regarding the clinical course of such potential findings in correlation with the development of HNSCC.

Methods:

The records of patients with FA evaluated and treated in the Dental Service and Head and Neck Service of Memorial Sloan Kettering Cancer Center from 2005 to 2017 were retrospectively reconciled. Clinical factors such as comorbid medical conditions, dental health, dental intervention, dental and oral sequelae of treatment as well as the presence of oral premalignant lesions (e.g. leukoplakias and erythroplakias) were reviewed.

Results:

A total cohort of 38 FA patients were treated at MSKCC and evaluated by the Dental and Head and Neck Services. At initial dental visit, the median age of the 38 FA patients was 12 years (range: 5 to 47 years). At the time of review, 16 (42%) patients were deceased. Co-morbidities included severe aplastic anemia, myelodysplastic syndrome, and acute myeloid leukemia. Pre-malignant lesions were noted in 10 patients. These lesions included leukoplakia and/or erythroplakia of the tongue, buccal mucosa, and gingiva. Subsequently, 3 of the 38 patients developed HNSCC (buccal mucosa/tongue). One patient presented with cervical squamous cell carcinoma.

Conclusions:

In our study, 30% of the patients with premalignant lesions developed HNSCC. This study highlights the importance for careful surveillance and routine dental maintenance of FA patients. All patients with FA must adhere to strict follow-up examination protocol and be monitored for premalignant lesions of the oral mucosa.

Newer Generation Oral Anticoagulants: An Unguided Increase in Popularity
*Tony Jaewon Kim, Bhavik Desai, Arwa M. Farag,
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Objectives:

Despite the recent and steady rise in the prevalence of newer generation oral anticoagulants (NGOA), there is no sufficient protocol or standard of care set for their uses. The primary objective of this study was to determine the prevalence of patients on NGOA at Tufts University School of Dental Medicine (TUSDM). The secondary objective was to investigate the current precautionary measures implemented when treating NGOA patients and postoperative complications associated with their use.

Methods:

TUSDM electronic record database system, axiUm, was retrospectively reviewed and patients on NGOA between 2010 and 2017 were identified. Among this population, charts of patients who underwent invasive dental procedures were further reviewed to investigate the preoperative and intraoperative precautionary measures taken and identify any postoperative complications that may be related to the use of NGOA.

Results:

A total of 132 patients were identified as taking NGOA at TUSDM, with their annual number steadily rising from 1 in 2011 to 52 in 2017. Among those, 64 patients underwent invasive dental procedures. Pre-treatment medical consults were obtained in all NGOA users undergoing invasive procedures, however, only 7 patients were instructed to discontinue their medication. Preoperative laboratory testing was not reported for any patient. Bleeding was controlled in 34 patients with the use of hemostatic agents, and 4 instances of post-operative complications; 2 blood clotting, 1 liver clotting and 1 delayed healing events were reported.

Conclusions:

The recent rise in the use of NGOA among patients receiving dental care warrants further attention and clear guidelines. While providers reported receiving medical consultations prior to dental treatment, there are no consistent patterns to the preoperative laboratory testing, discontinuations of drugs, and usage of perioperative precautionary measures. Expert consensus may be of great importance to develop well-established practice guidelines in this area. Moreover, although the incidence of postoperative complications associated with aggressive dental procedures was low and unlikely related to NGOA, drawing conclusion about drug safety based on this preliminary study is unfeasible. Further investigations with larger sample size and comparison of safety profile of NGOA with warfarin are needed.

#20 – 4:30-4:40pm
A Retrospective Analysis of the Clinicopathologic Risk Factors for Recurrence in Early Stage Oral Cancer
*Yingci Liu, Kurt Summersgill, Satish Kumar,
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Objective:

Oral squamous cell carcinoma (OSCC) is a life-threatening disease that can cause significant morbidity and mortality. OSCC recurrence occurs frequently with the rates varying between 12% and 40% depending on tumor stage. Our aim was to determine association between select clinicopathologic factors and the risk of local recurrence in early stage OSCC.

Methods:

After approval by University of Pittsburgh IRB (PRO17100554), we retrieved 29 cases of T1N0 stage OSCC over a period of 9 years (2004-2013). Cancer originating from non-mucosal epithelium and HPV-related lesions were omitted from our study. 19 cases experienced local recurrence within 5 years from the date of initial treatment, and 10 cases with no recurrence served as controls. Negative surgical margins were confirmed on all 29 cases. Relevant clinicopathologic data collected included sex, age, oral site, history of dysplasia, and surgical treatment modality (excision vs excision + neck dissection).

Results:

The majority 79.3% (23/29) of the T1N0 lesions were classified as well-differentiated tumors. The tongue was the most prevalent site (41.3%,12/29) and possessed the lowest rate of recurrence (50%, 6/12). The average age of the recurrence group was 64.7 years, while the control group was 59.7. Importantly, a higher risk of recurrence was found to be associated with a previous history of dysplasia (OR 15.4, 95% CI 1.6, 148.8, $p < 0.05$). In addition, recurrence was noted to be similar in both genders and surgical treatment modalities.

Conclusion:

Our present data, within its limitations, suggest that a history of dysplasia is associated with a higher risk of recurrence. Surgical excision along with neck dissections do not appear to decrease risk of recurrence in early stage cancers. Dental professionals hold a unique position in their proficiency of oral lesions and ability to follow up with patients with dysplasia at frequent intervals. As OSCC increases in frequency with age, understanding of the clinicopathological risk factors associated with recurrence will aid in improving follow-up protocols for oral cancer patients.

#21 – 4:40-4:50pm
Clinical Investigation on Oral Lichen Planus Occurred in Patients with Chronic Hepatitis C Virus Infection
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Objectives:

It is known that chronic hepatitis C virus (HCV) infection is complicated with various kinds of extrahepatic lesions. In the recent years, more studies suggested oral lichen planus (OLP) is one of extrahepatic lesions of chronic HCV infection. The purpose of this study is to evaluate the characteristics of OLP occurred in patients with chronic HCV infection.

Methods:

A retrospective chart review was carried out with 178 individuals with OLP, of whom 24 and 154 had been presented with (HCV-positive group) and without (control group) chronic HCV infection, respectively. OLP was diagnosed both clinically and histopathologically, and HCV infection was confirmed by serological tests for circulating anti-HCV antibodies. In the both groups, sex, age, involved site, clinical types, response to treatment, and malignant transformation rate were examined.

Results:

There was no significant difference of the sex, age, and involved site between the both groups. The ratio of ulcerative type was higher in the HCV-positive group than the control group. The proportion of reticular, ulcerative, erythematous, and plaque types in the HCV-positive group was 51.3%, 40.5%, 5.4%, and 2.7%, respectively, whereas, 62.0%, 17.4%, 11.3%, and 9.1% in the control group, respectively. All patients were treated by topical administration of betamethasone phosphate. As response to the treatment, the rate of full remission and improvement in the HCV-positive group was 27.0% and 67.5%, respectively, whereas 15.7% and 53.7% in the control group, respectively. The rate of relapse was 20.8% and 8.4% in the HCV-positive and control groups, respectively. The number of malignant transformation cases was 2 (8.3%) and 5 (3.2%) in the HCV-positive and control groups, respectively.

Conclusions:

The long-term follow-up is necessary because the relapse and malignant transformation rates in the HCV-positive group are higher than the control group.

Single Nucleotide Polymorphisms of VEGF and HIF-1alpha in Oral Submucous Fibrosis: A pilot study

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Objectives:
Oral Submucous Fibrosis (OSMF) is a potentially malignant oral disorder with high transformation rate into Oral Squamous Cell Carcinoma (OSCC). OSMF is characterized by severe sub-mucosal fibrosis and decreased vascularity leading to tissue hypoxia. Tissue Hypoxia is known to induce HIF-1 α and VEGF expression leading to angiogenesis which has been implicated in development of OSCC.
Several Single Nucleotide Polymorphisms (SNPs) of VEGF A, VEGF C and HIF-1α have been implicated in increased susceptibility to OSCC , poor survival rates, vascular invasion and increased tumour size and can act as a prognostic marker. Currently there is no reliable marker to predict malignant potential in OSMF. This pilot study aims to determine the frequencies of SNPs of VEGF A, VEGFC and HIF-1α in OSMF and explore their potential as a biomarker for malignant transformation

Methods:
The frequency of SNPs of VEGF A (1154 GG, 936CT), VEGF C (rs7664413, rs2046463) and HIF-1α (C1772T, G1790A) in 150 samples (50 OSMF, 50 OSCC, 50 Healthy controls) were determined by Allele specific / RFLP PCR technique using standard protocol. Mann-Whitney set was used to determine differences between the groups. Odds ratio and Relative Risk was calculated to identify the association of polymorphism with the disease.

Results:
The heterozygous form of VEGF-A 936CT was significantly increased in OSCC in comparison to controls with a relative risk of 4.63 ($p<0.01$). Heterozygosity of VEGF-A 936CT was also increased in OSMF but non-significantly.
Both heterozygous and homozygous allele of VEGF-C rs1485766 were found to be significantly increased in OSMF and OSCC in comparison to controls (relative risk of 2.68 & 8.67 in OSMF, relative risk of 3.34 & 11.27 in OSCC respectively).
Heterozygous allele of HIF-1α C1772T and G1790A SNP were also found to have significant positive association with OSMF and OSCC as compared to controls ($p<0.001$).

Conclusions:
The frequencies of SNPs of VEGF and HIF-1α were found to be significantly increased in OSMF and OSCC. The SNPs have potential to act as a prognostic biomarker and may also be used for the development of specialized anti-VEGF/ HIF-1α drugs in the treatment and prevention of OSCC in OSMF