# Oral Abstracts Session I
## Thursday, 05/23/2018, 1:00pm-2:30pm

# = Presentation 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

**Level of Dental Disease and Differences in Dental Treatment in Stem Cell Transplant Patients: OraStem Study**

*Lara Napodano, Inger von Bültzingslöwen, Allan Hovan, Marie Charlotte Huysmans, Judith E. Raber-Durlacher, Bengt Hasseus, Nicole Blijlevens, Alexa Laheij, Karen Garming Legert, Nigel Rozario, Anna Osipoff, Jan-Erik Johansson, Waylon Howard, Michael T. Brennan
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**Objectives:**

There lacks an accepted standard of care for dental treatment prior to hematopoietic stem cell transplant (HSCT). Therefore, in this international, prospective multicenter study (OraStem), we evaluated differences in dental disease, oral hygiene practices and dental treatment completed prior to HSCT.

**Methods:**

Enrollment sites include Vancouver, BC(Canada); Gothenburg (and Huddinge, (Sweden); Nijmegen and Amsterdam (The Netherlands) and Charlotte, NC (USA). The frequency of dental disease, oral hygiene practices and dental treatment prior to HSCT are reported.

**Results:**

The number, mean age, gender(%) of the cohort included: overall n=269, 53.6 years, male=56%; Vancouver n=58, 52.3 years, male=57%; Sweden n=29, 57.2 years, male=56%; Nijmegen n=81, 55.1 years, male=54%; Amsterdam n=43, 55.2 years, male=59%; Charlotte n=58, 49.6 years, male=57%. Overall, the most frequent medical diagnoses necessitating HSCT: Myeloma=74(27%), Acute myelogenous leukemia (AML)=67(24%); Lymphoma=37(13%), Myelodysplastic syndrome (MDS)=19(7%); Acute lymphoblastic leukemia (ALL)=17(6%). Majority of transplants overall were allogeneic(61%) versus autologous(36%). Patients reporting brushing two or more times/day: Overall=200(73%); Vancouver=40(67%); Sweden=27(87%);ZX Nijmegen=63(78%); Amsterdam=34(77%); Charlotte=36(59%). The number of patients reporting seeing a dentist or dental therapist routinely: Overall=202(73%); Vancouver=41(71%); Sweden=24(77%); Nijmegen=70(86%); Amsterdam=37(84%); Charlotte=30(49%). Conditions of teeth were recorded before and after dental treatment prior to HSCT. Upon enrollment, the mean number of teeth with a natural root (with or without crown): Overall=24.2; Vancouver=23.2; Sweden=26.3; Amsterdam=23.5; Nijmegen = 23.8; Charlotte=25.5. The number of people who underwent tooth extraction and number of dental extractions (% of existing teeth) before transplantation: Overall=44, 126 teeth(0.5%); Vancouver=4, 5 teeth(0.1%); Sweden=5, 28 teeth(0.32%); Nijmegen=10, 41 teeth(0.5%); Amsterdam=8, 14 teeth(0.3%); Charlotte=17, 59 teeth(1.0%). The number of teeth with periodontal pocketing >5 mm left untreated: Overall=102(0.4%); Vancouver=23(0.5%); Sweden=25(0.3%); Nijmegen=25(0.3%); Amsterdam=12(0.3%); Charlotte=35(0.8%). The number of teeth with one or more carious lesions to dentin left untreated: Overall=246(1.0%); Vancouver=11(0.2%); Sweden=27(0.3%); Nijmegen=118(1.5%); Amsterdam=11(0.3%); Charlotte=99(1.7%).

**Conclusions:**

This baseline report reveals variations in dental disease, oral hygiene practices and dental treatment rendered prior to HSCT among different study centers. Establishment of an international standard of care for dental treatment prior to HSCT is needed. Prospective OraStem study data will increase understanding of risk factors related to oral complications during HSCT.

**#2:**
**Phylogenetic Analysis of Human Papillomavirus Proteins**

*Takaaki Kamatani, Tatsuo Shirota
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**Objectives:**

Human papillomaviruses (HPVs) have evolved over millions of years, with over 200 serotypes already identified. HPVs cause oral, cervical, and any other keratinocyte cancers and are of two groups based on the risk of carcinogenesis; high-risk and low-risk HPVs. Differences in the evolution of high-risk and low-risk HPVs and their association with carcinogenesis in accordance with each protein expressed by HPVs are unclear. To reduce oral carcinogenesis by HPVs, information regarding evolutionary changes in HPV proteins and the mechanism underlying the acquisition of the ability for oral carcinogenesis of HPVs is needed. This study aimed to evaluate the carcinogenic potential of HPVs via phylogenetic analysis of HPVs proteins.

**Methods:**

Eight proteins of alpha HPVs were selected, namely, E1, E2, E4, E5, E6, E7, L1, and L2. The complete amino acid sequences of these eight HPV proteins were downloaded from the UniProtKB. HPVs were classified into two groups on the basis of high and low clinical risk for cancer in accordance with the International Committee on Taxonomy of Viruses (ICTV).

Phylogenetic analysis of HPV genomes was performed using Molecular Evolutionary Genetics Analysis version 7 (MEGA7) and the neighbor-joining algorithm. Bootstrap analysis of 1000 replicates was performed on each tree to determine the confidence levels.

Fisher's exact test was performed for statistical analysis, with $P<0.05$ (two-sided) indicating statistical significance.

**Results:**

Each protein from different HPV strains consistently showed evolutionary divergence into distinct lineages. Multiple sequence alignment revealed amino acid profiles showing conserved independent lineage specific substitutions. Phylogenetic analysis revealed that HPV proteins evolved in a similar manner.

**Conclusions:**

The present results provide an overview of the characteristics of HPV proteins and their evolutionary changes, potentially explaining the pathogenesis of oral cancer due to HPVs.

**#3**

**The Evaluation of Sequential type / de novo type in 100 Cases of Oral Squamous Cell Carcinoma**

*Rie Kawashima, Yoshinori Jinbu, Naruo Okada, Junichi Hayasaka, Tadahide Noguchi, Yoshiyuki Mori
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**Objectives:**

Oral Potentially Malignant Disorders (OPMDs) has been suggested for oral precancers, including both oral precancerous regions and oral precancerous conditions. Oral squamous cell carcinoma (OSCC) is divided into two types by the appearance of the cancer regions. One is carcinomas with precancerous white lesions; sequential type. The other is accompanied SCC without pre-cancerous white lesions; de novo type.The aim of this study was to evaluate clinicopathological characteristics in sequential type and de novo type in OSCC.

**Methods:**

We analyzed 100 cases of OSCC of the tongue diagnosed at Jichi Medical University. We divided these OSCC cases into two types using the intraoral photographs by an oral surgeon. Statistical analysis was done by Chi-square test (P<0.05).

**Results:**

In 100 cases, there were 51 cases of sequential type (51%) and 49 cases of de novo type (49%). The percentage of T1+T2 group (92.2%) in the sequential type was considerably higher than those of T3+T4 group (7.8%). In de novo type, T1+T2 group showed 77.6% and T3+T4 group showed 22.4%. The percentage of the lymph node metastasis in the negative group (84.3%) in sequential type was higher than those of the positive group (15.7%). In de novo type, the lymph node metastasis negative group showed 65.3% and the positive group showed 34.7%. These were significant differences. Regarding the postoperative lymph node metastasis and Yamamoto-Kohama classification of the mode of invasion, there were no significant differences in sequential type and de novo type. In regard to the pathological findings, the margin of the cancer lesions in sequential type tended to be connected to dysplasia or OIN. It also showed the unclear margin. On the other hand, it showed the clear margin in de novo type.

**Conclusions:**

In this study, we found that the patients with sequential type tended to visit hospital in T1+T2 early stages and to have no lymph node metastasis, compared with the cases of de novo type. Our results suggested that there was a relationship between sequential type and OPMDs.

**Topical Zinc Ora-base (5%) In Reducing The Oral Mucositis During Cancer Chemo Radiotherapy**

Sourab Abhyankar, *Kavya Alluri, Pundarikakshaiah Deveneni, Jayasurya Kondapaneni, Chaitanya Nallan CSK, Sri Laxmi Manasa Penmetsa
Panineeya Mahavidyalaya Institute of Dental Sciences and Research Centre, India;

## Objectives:

Oral mucositis is a painful sequalae of the cancer chemo-radiotherapy affecting the oral mucosa. Several studies have shown that Zinc could reduce the severity of oral mucositis. However, the zinc formulations are available only in the form of tablets, which posed difficulty in administration during oral mucositis. The present study was aimed to compare and evaluate the efficacy of topical zinc and improvised zinc ora-base in the treatment of oral mucositis.

## Methods:

The study was conducted at MNJ Regional Oncology Centre among 75 patients. It was a single centre, single blinded, randomized trial in which, 50 patients were case clusters & the remaining 25 patients were under controls. Case group were randomly divided into two groups, with 25 patients belonging to Group A, who received topical oral 5% Zinc paste, Group B consisting of 25 patients who received combination of topical oral 5% Zinc paste with improvised zinc preparation TID for 35 days. 25 patients under controls were prescribed standard treatment of the cancer hospital. The groups were assessed for mucositis by WHO grading system at 7th, 14th, 21st, 28th, 35th day respectively.

## Results:

An overall comparison between the groups and severity of oral mucositis revealed that there was statistically significant difference observed between all the groups compared to controls (ANOVA) and also between intergroup. Chi-square test Zinc orabase performed better during 35th day compared to controls, 0.037 ($p < 0.05$), improvised preparation of zinc had shown near significance during 7th, 21th and 35th day of the therapy. The improvised zinc performed better than the zinc alone during 21st and 35th days 0.029, 0.013 ( $p < 0.05$).

## Conclusions:

To conclude, the severity of oral mucositis decreased in both the zinc intervention groups but the improvised Zinc paste (5%) showed overall decrease in severity of oral mucositis. Further study with high sample size was necessary to establish this formulation for oncology practise.

**Enhanced Proliferation and IL-6 secretion of T Cells Mediated by Over-expression of TRIM21 in Oral Lesions of Patients with Oral Lichen Planus**

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## Objectives:

To screen the interacting proteins of TLR9 and to explore the function of TRIM21 overexpression.

## Methods:

Buccal mucosa samples and PBMCs were collected from both OLP and healthy control groups for the following studies: (1) CoIP followed by mass spectrometry to screen interacting proteins of TLR9 in OLP lesions; (2) immunofluorescence co-localization analysis and plasmid transfection plus CoIP were used to verify the protein interaction; (3) qPCR used to quantify its gene expression; immunohistochemistry used to delineate its spatial distribution; (4) overexpression of this gene in T cells to test its function.

## Results:

(1) Among 7 potential TLR9 interacting proteins predominantly presented in OLP samples, TRIM21 was selected as objective for further study; (2) immunofluorescence co-localization analysis and plasmid transfection plus CoIP were not able to verify the interaction of TRIM21 and TLR9; (3) significantly higher transcription of TRIM21 was revealed through qPCR; a larger amount of TRIM21 positive cells mainly infiltrated in the lamina propria of OLP lesions than those of healthy control group by immunohistochemistry; Gradually upward tendency of TRIM21 expression in T cells was found among PBMCs, lymph nodes and OLP lesions; (4) TRIM21 overexpression significantly enhanced proliferation and IL-6 secretion of T cells.

## Conclusions:

Significantly high expression of TRIM21 in OLP lesions may be of great significance in OLP immunopathological mechanism. Overexpressed TRIM21 in OLP lesions is more probably a primary pathogenic molecule.

**#6:**

**Analysis of Clinical Oral Medicine Practices at the University of Pennsylvania: A 5-year Retrospective Study**

*Matthew Sun, Thomas P. Sollecito, Martin S. Greenberg, Andres Pinto, Eric T. Stoopler
University of Pennsylvania School of Dental Medicine, USA

**Objectives:**

The aim of this study was to describe the cohort of oral medicine (OM) patients, characterize OM clinical practices at the University of Pennsylvania (Penn), and inform training for future OM specialists.

**Methods:**

Non-probability sampling of OM resident patient logs for all Penn OM patients presenting for clinical care from 2008 to 2013 was conducted after obtaining IRB approval. Patient data was filtered by inclusion criteria and data validation was implemented to exclude redundant and inconclusive entries from analysis. OM resident patient logs included clinical diagnosis, International Classification of Diseases, 9th edition (ICD-9) code, medical history, clinical procedure, Current Procedural Terminology (CPT) code, attending physician, and resident participation notes. For outpatient OM medical practices, diagnoses were classified into domains of oral mucosal diseases, salivary gland dysfunction, orofacial pain, oral chemosensory disorders, and other head and neck pathologies. For hospital inpatients consulted by the OM service, admitting medical diagnoses were grouped into associated medical disciplines. Procedures performed in outpatient OM medical practices were also catalogued. For the outpatient OM dental practice, patient comorbidities were categorized by medical discipline. Frequency and percentages were tabulated for clinical diagnoses/ICD-9, medical history, and clinical procedures/CPT. Additional data was analyzed with descriptive statistics.

**Results:**

Outpatients in OM medical practices (n=6024) averaged 1.56 diagnoses from OM specialists. Orofacial pain (45.02%) and oral mucosal diseases (34.28%) comprised the majority of OM diagnoses followed by salivary gland dysfunction (6.09%), oral chemosensory disorders (5.61%), and other head and neck pathologies (5.55%). The most frequent procedures performed were tissue biopsies (59.34%) and treatments for temporomandibular disorders (29.9%). Hospital inpatients (n=313) comprised 3.46% of Penn OM patients in which cardiovascular disorders (38.99%) were the most common admitting medical diagnoses followed by leukemias (12.2%) and hematologic diseases (6.85%). In the OM dental practice (n=1648), 42.05% of outpatients presented with a median of 3 medical comorbidities (range= 2-11) in which cardiovascular (27.13%) and immunodeficiency disorders (16.67%) were most prevalent.

**Conclusions:**

Analysis of Penn OM clinical practices emphasizes the breadth and multidisciplinary nature of OM services as well as the importance of comprehensive postdoctoral training in all domains of OM for future OM specialists.

**Comparative Study On The Efficacy Of High Dose Oral Ascorbic Acid With/without Zinc In Reducing The Severity Of Oral Mucositis During Cancer Chemo-Radiation**

*Nallan CSK Chaitanya, Arvind Muthukrishnan, Jayasurya Kondapaneni, Alluri Kavya, Abhyankar Sourab, Deveneni Pundarikakshaiah, Humaira Samreen, Yarram Rajanikanth, Hafsa Abdul hameed
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## Objectives:

Anti-oxidants may control severity of oral mucositis during cancer treatment. A well-designed trial to investigate oral vitamin C that reduce the severity of oral mucositis was warranted. This study aimed to investigate and compare the effect of oral ascorbic acid 4mg alone or in combination with zinc 50 mg on the oral mucositis during chemo-radiotherapy by WHO grading & to evaluate pain & taste perception among the participants during of the treatment.

## Methods:

A prospective randomized controlled single blinded single centre trial was conducted on 180 participants, diagnosed with oral & oro-pharyngeal cancers, treated by chemo radiotherapy. Participants were categorized into 2 major groups controls (Group A) and test group (Group B). Test group with 120 subjects, divided into three subgroups. Group B - 60 subjects received oral ascorbic acid 1 gram 4times daily, Group C- 30 subjects received zinc acetate 50 mg twice daily & Group D - 30 subjects received the combination of zinc & Vitamin C. The control group (60 subjects) received standard protocol for oral mucositis of the hospital. Severity of oral mucositis was assessed by WHO grading at weekly intervals 7th,14, 21st, 27th & 35th days. Pain on vas scale and taste perception were enquired.

## Results:

Significant difference was observed between mucositis grades (p<0.001) in both experimental and control group during treatment. Friedman ($\chi2$ = 223.837, 151.714, 84.289 and 80.856) Student-Newman-Keuls method showed statistical significant difference between all multiple comparisons and intervals. Intervention with vitamin c lead to decrease in severity of oral mucositis by the end of week 5. Kruskal- Wallis one-way ANOVA for pain at day 35 showed no statistical difference between study groups (P= 0.204). Chi-square test on 35th day, all participants from controls and vitamin C had loss taste sensation but preserved in zinc groups.

## Conclusion:

Zinc with vitamin C or Zinc alone had demonstrated significant decrease in the severity of oral mucositis compared to vitamin c alone. The pain decreased with vitamin C supplementation when compared to controls. Vitamin C use reduced pain perception and zinc reduced mucositis scores. A combination of these benefits in pain, mucositis reduction and taste preservance.

**#8:**

**Spontaneous Osteoradionecrosis- Features and Characteristics: The Memorial Sloan Kettering Cancer Center Experience**
*Dalal Alhajji, Yoon Ah Danskin, Bridget O'Hara, Karl Armand Solano, Jessica Flynn, Elyn Riedel, Sae Hee Kim Yom, Cherry Estilo
Memorial Sloan Kettering Cancer Center, USA

## Objectives:

Osteoradionecrosis (ORN) is a complication of head and neck radiation therapy (RT) that is associated with significant morbidity. The incidence of ORN is variable, and it has been speculated to be lower with advanced RT techniques. Risk factors that have been associated with developing ORN mainly include trauma and a radiation dose to the head and neck region >60 Gy. However, in a study conducted by our group, ORN developed spontaneously (without any known history of trauma or dentoalveolar procedure) in 82% of the ORN-cohort following intensity-modulated radiation therapy (IMRT).The purpose of this study is to characterize spontaneous ORN and to compare spontaneous ORN to non-spontaneous (eg, related to trauma or dentoalveolar procedures) ORN.

## Methods:

Following approval by the Institutional Review Board of Memorial Sloan Kettering Cancer Center (MSKCC), the treatment records of 44 patients with spontaneous ORN (Group A) and 24 patients with non-spontaneous ORN (Group B) treated with IMRT at MSKCC for head and neck cancer (HNCa) were identified and retrospectively reviewed. Average prescribed mean and maximum radiation doses for the region of ORN were calculated by using MSKCC's proprietary radiation treatment planning software. Furthermore, Fischer exact tests were used to compare patient characteristics, such as primary site, tumor stage, smoking status, and other comorbidities, between spontaneous ORN patients and non-spontaneous ORN patients.

## Results:

Preliminary data from 12 patients in Group A and 6 patients from Group B suggests that patients in Group A appear to have been exposed to higher radiation doses (Dmax) >70Gy compared to Group B. Furthermore, no statistical significance was noted between the 2 groups for primary tumor, tumor stage, smoking status, and comorbidities such as cardiovascular disease and hypertension ($p>0.05$). However, a statistical significance was evident for diabetes in Group B ($p<0.05$).

## Conclusion:

Collection of data on the expanded cohort of patients from each group, as well as other variables, such as radiation therapy fractionation is ongoing. Our initial data indicates that increased radiation dose >70 Gy may be associated with development of spontaneous ORN.

**Salivary Proteins As Markers Of Radiation-Related Oral Mucositis**

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## Objectives:

To characterize the salivary proteomic profile of patients treated for head and neck cancer (HNC) aiming to correlate the salivary proteomic profile with the risk of developing severe radiation-related oral mucositis (OM).

## Methods:

41 oral squamous cell carcinoma (OSCC) patients submitted to adjuvant radiotherapy (RT) or chemoradiotherapy (CRT) were included. All patients were submitted to dental conditioning protocols previous to RT treatment. OM and OM-related pain were daily evaluated during RT and graded according to the Common Toxicity Criteria for Adverse Events (NCI, Version 4.0, 2010) and the Visual Analogue Scale (VAS). For the molecular analysis, whole saliva was collected immediately prior to RT and subjected to proteomic by means of liquid chromatography coupled to mass spectrometry (LC-MS/MS) (LTQ Orbitrap Velos MS/ Thermo Fisher Scientific, Bremen, Germany) and label-free protein quantification. The results obtained from the targeted proteomic analysis were compared to OM clinical outcomes. Statistical analysis was performed using the Wilcoxon test.

## Results:

73% of patients presented stage III/IV OSCC. 58% were submitted to CRT protocols with a mean RT dose of 66Gy. Most of the patients (66%) presented visible tumor areas at the moment of saliva collection. 43.9% presented grade 2 and 31.7% presented grade 3 as highest OM grade during RT with a mean highest reported VAS of 3.53. For the target proteomics analysis, a total of 65 proteins were observed mostly related to biological processes, such as immune responses, peptidase inhibitor activity, and inflammatory system. The Macrophage migration inhibitory factor (MIF HUMAN) was statistically significant when correlated to OM grade. MIF was observed in patients with grade 1-4 OM and presented higher abundance for OM grades 3 and 4 when compared to grades 1-2 (p=0,04).

## Conclusions:

The correlation of MIF with the severity of OM is compatible with the role of MIF as a proinflammatory protein. This seems to be the first study to describe this association, therefore, future prospective studies would be ideal to observe pre- and post-RT alterations in salivary MIF levels in order to validate this result and better understand the role of MIF in the pathogenesis of OM.

## #10:
## Endometriosis Increases The Risk For Sjogren's Syndrome: A Nationwide Prospective Cohort Study

*Kevin Ma
University of Pennsylvania, USA

**Objectives:**

Sjögren's syndrome (SS) is an autoimmune disease with oral manifestations. SS may result in hormonal imbalance and immune dysfunction, and its occurrence could relate to comorbidities including endometriosis. The prevalence of endometriosis in women with chronic pelvic pain is higher than 33%, and in SS patients the prevalence is 6.3%. Given the limited existing studies, we sought to determine whether endometriosis patients have higher risk of SS.

**Methods:**

We performed a prospective cohort study of females with newly diagnosed endometriosis from 1999 to 2013 from the Longitudinal Health Insurance Database (LHID). Data on age, history of underlying comorbidities were retrieved from LHID. Data on the use of corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) were also compared. A total of 16,214 patients were identified to have endometriosis. Among them, 15,949 patients received a diagnosis of SS after the index date, and were included for analysis. 31,880 (7.10%) of 448,953 eligible patients without a history of endometriosis were recruited as age-matched controls. A Cox proportional hazard model was developed with a priori dichotomous variable of endometriosis, aiming to estimate the risk of SS in patients with endometriosis. A cumulative probability model was adopted to assess the time-dependent effect of endometriosis on the development of SS, implying the casual link of the association. Sensitivity analysis was conducted to further confirm the risk of SS in endometriosis patients.

**Results:**

The mean ± SD age (38.8 ± 8.8 y/o) was the same for patients with or without endometriosis (p = 0.406). The Cox proportional hazard model analysis showed that patients with endometriosis were more likely to have SS than patients that didn't develop endometriosis (adjusted hazard ratio =1.5, 95% CI =1.27–1.77, P < 0.05), which persisted in a sensitivity analysis (adjusted HR=1.34, 95% CI = 1.04–1.74, P < 0.05).

**Conclusions:**

Our findings suggest an association between endometriosis and a higher risk of developing SS. Endometriosis may be a risk factor for, or share a common cause, with SS. This is the first study with extended follow-up that address both the timing and development of SS in patients with endometriosis.