EARLY-PHASE DEVELOPMENT OF SALIVARY PROangiogenic CYTOKINES AS BIOMARKERS IN LEUKOPLAKIA CLINICAL TRIALS. Nelson L. Rhodes, Eva Szabo, Beverly Wuertz, Kate Cole, Joe Rohrer, and Frank Ondrey, University of Minnesota, Minneapolis, MN, USA.

Objectives. A significant emphasis has recently developed as to the potential utility of minimally or noninvasive surrogate end points in head and neck cancer clinical trials. Consequently, biomarkers analysis in saliva is an attractive area of investigation in oral cancer. Our laboratory (and others) has demonstrated the upregulation of NF-κB-dependent cytokines (IL-6, IL-8, VEGF) in squamous cell carcinoma (SCC) cell lines, animal models and oral cavity fluids from patients. The goal of this study was to quantify 3 NF-κB-dependent cytokines (IL-6, IL-8, VEGF) in the saliva (and other oral fluids) of patients undergoing clinical trials for the intervention of oral leukoplakia.

Material and Methods. Twenty-one patients with oral leukoplakia (biopsy-proven moderate-severe epithelial dysplasia) were enrolled, examined, and their lesions measured. We collected whole unstimulated saliva, along with an isotonic saline rinse and serum. IL-6, IL-8, and VEGF were analyzed in triplicate by ELISA (by methods which we have previously reported). The patients were then enrolled in a 12-week clinical trial of a ppar-gamma agonist for treatment of the leukoplakia.

Results. The results indicated up to a 10-fold increase in saliva as compared with serum for all 3 cytokines. IL-6 was considerably lower than IL-8 or VEGF and comparable with levels in cell lines. IL-8 and VEGF were coordinately significantly upregulated in saliva (P < .0001). There were modest correlations between the cytokine levels and lesion size (P < .05).

Conclusions. We conclude that these NF-κB-dependent cytokines (IL-6, IL-8, VEGF) are produced in oral SCC and preneoplastic leukoplakia and therefore found in the local milieu (saliva and fluids). The correlative science between SCC cell lines and saliva in oral leukoplakia strengthens the case for further use of these biomarkers in oral carcinogenesis studies and lesion monitoring in clinical trials.

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HIGH CONCENTRATION OF MINOCYCLINE RINSES FOR CONTROLLING RECURRENT APHTHOUS STOMATITIS. Noam Yarom, Keren Zelig, and Meir Gorsky, Sheba Medical Center, Tel Hashomer, Israel.

Objectives. In previous studies, we demonstrated the beneficial effect of minocycline 0.2% mouthwash on symptoms associated with recurrent aphthous stomatitis (RAS) when compared with those of placebo or tetracycline. The purpose of this study was to compare the efficacy of 2 different concentrations of minocycline water solution mouthwashes on the symptoms associated with RAS.

Methods. The study was designed as a prospective, randomized, double-blind, crossover study. Twenty-nine RAS patients who fulfilled the entry criteria were enrolled using minocycline mouthwashes of 2 different concentrations: 0.2% and 0.5%. The patients were randomly instructed to use 5 mL of minocycline water solution mouthwashes 4 times a day, initiating the treatment at the point of the prodromal symptoms of aphthous ulcers. A washout period of 4 weeks was needed before using the other concentration. The intensity of symptoms, using the visual analog scale of 0 to 10, and adverse reactions were recorded by each individual at the end of each day of treatment.

Results. Of 21 patients who experienced RAS during the study period, only 14 experienced 2 episodes and completed the whole protocol of the study. The intensity of pain associated with RAS was significantly lower when the higher minocycline concentration was used, reaching a level of statistical significance as soon as the fourth day of treatment (P = .017). The mean duration of RAS-associated pain was significantly shorter (4.07 vs 5.64 days; P = .02) and healed sooner (5.64 vs 6.85 days; P = .011) when the higher concentration was used. No adverse reactions were reported by the patients.

Conclusions. The higher concentration of minocycline mouthwash (0.5%) is significantly more efficient for controlling RAS than the 0.2% concentration, as tested in our previous studies.

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Objectives. High-dose melphalan followed by an ASCT is standard initial therapy for MM. Oral mucositis is a potentially severe complication of this treatment. We hypothesized that obesity and renal insufficiency modulate the pharmacokinetics of melphalan and, therefore, affects the severity of oral mucositis.

Methods. Thirty-nine patients with MM undergoing high-dose melphalan followed by ASCT were evaluated. Patients received melphalan on day –2 at a dose of 200 mg/m2 and ASCT on day 0. We assessed body composition using DEXA and renal function using 24-hour urine creatinine clearance. We assessed toxicity on day +7 using the OMAS. We also assessed patient-reported symptom scores using the MDQ periodically during the first month.

Results. The median age was 55 years (range 37-70) and 59% were male. The median percentage body fat as measured by DEXA was 31% (range 15%-53%), and the median GFR was 105 mL/min (range 28-194). In a multivariable linear regression model, including percent body fat, weight, GFR, and actual melphalan dose, we observed a correlation between OMAS score and percent body fat. In a similar multivariable model, including percent body fat, weight, GFR, and actual melphalan dose, we observed a correlation between MDQ score and percent body fat.

Conclusions. More obese patients, as measured by percent body fat, have more severe oral mucositis after high-dose melphalan, independent of melphalan dose, weight, and renal function.