INTERCEPTOR
INTERCEPTION OF ORAL CANCER DEVELOPMENT

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OPMDay

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ABSTRACT BOOK

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FACULTY OF MEDICINE - UNIVERSITY OF PORTO

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Abstract selected talks

Artificial Intelligence-based Oral Cancer Diagnosis from mRNA Biomarkers: Multicohort Validation and Demographic Generalization

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Purpose: Aim to validate the AI based Oral cancer diagnostic model on Mulltidemographic cohort
Method: Utilizes AI to diagnose oral cancer, analyzing mRNA biomarkers, conducting multicohort validation, and employing ML algorithm
Results: This study explores using Artificial Intelligence (AI) to diagnose oral cancer based on the expression levels of 14 messenger RNA (mRNA) biomarker genes namely HOXA7, CENPA, NEK2, DNMT1, INHB, FOXM1, TOP2A, BIRC5, MMP13, IL8, NR3C1, IVL, CBX7 and S100A16 in 443 samples. The aim is to create a diagnostic AI model for the accurate classification of cancer samples and highlight the performance of the external validation on different demographics to ensure the generalisability and confidence of the model.
An international multicohort validation was conducted on UK patient samples (n=309), achieving 93% accuracy. Before remodelling, diagnostic accuracies for Chinese head and neck squamous cell carcinoma (HNSCC; n=35) and nasopharyngeal squamous cell carcinoma (NPSCC; n=62) cohorts were 94% and 66% respectively. Accuracies for North Indian (n=48) and South Indian (n=33) HNSCC cohorts were 75% and 21% respectively.
For remodelling, Chinese and Indian cohorts were combined into two primary datasets. Data imputation for missing values was done before normalization. Imbalanced data distribution in the Chinese dataset (29 regular and 68 cancer) was rectified using oversampling techniques. Missing values were handled and scaled using Min-Max Scalar. Class imbalances were addressed using SMOTE, followed by training multiple machine learning models: linear Regression, Support Vector, XGBoost, Random Forest, Decision Tree, and Gaussian Naive Bayes paired with Grid Search cross-validation. Hyperparameters were tuned to prevent overfitting.
Conclusion: The Random Forest classifier performed best for the Chinese dataset, achieving 85% accuracy and 77% F1 score after SMOTE. XGBoost followed closely with 80% accuracy and 67% F1 score. In the Indian dataset, both Random Forest and XGBoost classifiers performed similarly, achieving 88% accuracy and 83% F1 score. This study thus underscores the performance of Curenetics' oral cancer diagnostic model and robustness across diverse demographic populations.

Immune-based Stratification and Evolutionary Biomarkers In Oral potentially malignant disorders (ISEBIO) – A retrospective EU multicentric study leveraging the INTERCEPTOR nework

Marine Benaïssa 1, Marie Sicard 1, Allon Irit 2, Amaral Mendes Rui 3, Benzerdjeb Nazim 4, Bertolus Chloé 5, Bouaoud Jebrane 5, Bouletreau Pierre 5, Bossi Paolo 6, Breuskin Ingrid 7, Carlier Adelaïde 4, Costea Daniela-Elena 8, Čēma Ingrida 9, Foy Jean-Philippe 5, Hunter Keith 10, Joshua Ben-Zion 2, Koljenović Senada 11, Khurram Ali 12, Le Tourneau Christophe 13, López Jornet Pía 14, López Pintor Muñoz Rosa María 21, Martin Joey 13, Ooft Marc 15, Poell Jos 16, Retel Valesca 17, Sapkota Dipak 18, Schmitt Fernando 3, Shlapobersky Mark 2, Shaw Richard 10, Soluk Tekkesin Merva 19, Thomas Steve 20, Varazzani Andrea 4, Pierre Martinez 1, Pierre Saintigny 1.

Context and purpose of the study

Oral squamous cell carcinomas (OSCC) represent the most common site of all head & neck squamous cell carcinomas globally, often diagnosed at advanced stage leading to significant and long-term morbidity. OSCC is preceded by Oral Potentially Malignant Disorders (OPMD) in 30% of the cases. Through ISEBIO, we hypothesize that gene expression profiling and genetic alterations may improve oral cancer risk assessment in patients with oral leukoplakia, erythroplakia or erythroleukoplakia (E-/L), the most frequent forms of OPMD in western countries. ISEBIO will test this hypothesis in a multicentric, retrospective pan-European cohort.

Proposed Method

We anticipate a total of 246 patients to retrospectively participate in the study, including 1/3 patients who progressed to OSCC and 2/3 of patients who did not progress to OSCC with at least 2-year follow-up. A centralized pathological review, comprising a panel of EU expert pathologists from the INTERCEPTOR network, will review all cases for sample qualification. Biological characterization will include immunohistochemistry for CK13 and CK17, DNA sequencing using the Agilent OneSeq Target Enrichment approach that includes a whole-genome “backbone” (300kb, copy number alterations) and a targeted sequencing panel (435kb panel based on the 62 HNSCC driver genes) and RNA sequencing using the 3’Tag-Seq (Lexogen) approach. Currently, 16 centres across Europe (11 countries from North (2), South (4), West (4), South-East (1)) participate to the study.

Conclusion and perspectives

ISEBIO aims to improve oral cancer-risk stratification over standard histopathological assessment for patients with OPMD. A secondary objective is to decipher the molecular heterogeneity of E-/L and help identifying actionable biological features to foster the development of precision prevention of oral cancer.

Early detection of OPMD and OSCC using mutation analysis of DNA in saliva and plasma

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Purpose: Clinical study to test saliva and plasma as tools for early detection of OPMD and OSCC.
Method: Detecting mutations using deep-sequencing of DNA from saliva/plasma of patients during follow-up of surveillance or treatment.
Results: Fanconi anemia (FA) individuals present more than 700 times the incidence of HNSCC in the general population, mainly in the oral cavity. Moreover, FA patients suffer from frequent and recurrent OPMDs difficult to diagnose and treat. A clinical prospective and longitudinal study collecting samples during a 3-year period of time demonstrated that FA patients having mutations in saliva/plasma display a higher risk of developing OPMD and OSCC. Interestingly, as most mutations were detected in saliva, this liquid biopsy was particularly informative in this context. Encouraged by these results, we initiated a clinical study on non-FA patients having advanced OSCC to test whether a similar approach could help detect early recurrent/metastatic disease after treatment. We are presenting the study design and preliminary results of the first 10 patients with a follow-up time of up to 1 year.
Conclusions: Liquid biopsies are less invasive than standard biopsies and can be easily and repeatedly collected over periods of time. Deep sequencing offers high sensitivity in detecting mutant DNA. Our analysis of saliva and plasma is a promising tool for the early detection of OPMDs and OSCC in high-risk populations. Future analysis could confirm whether the tool is useful in the setting of advanced OSCC.

Raman spectroscopy for identification and monitoring of oral potentially malignant disorders

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Purpose: This presentation will discuss our recent and current work on Raman spectroscopy for identification of OPMD.
Method: Raman spectroscopy was used to detect biochemical changes in FFPP tissue, brush biopsies and saliva.
Results: Using FFPP tissue sections, we showed the ability of Raman spectroscopy to discriminate between benign oral lesions and mild, moderate and severe dysplasia. We also showed good discrimination between oral exfoliated cells (brush biopsy) from patients with oral leukoplakia (OLK) and healthy volunteers, differentiation of low (no and mild dysplasia) and high risk (moderate and severe dysplasia) OLK and the detection of field cancerisation. Similarly for saliva samples, we demonstrated discrimination between patients with OLK and healthy volunteers and differentiation between low and high risk OLK. Our current study is focussed on monitoring the progression of OPMD in patients using Raman spectroscopic analysis of minimally invasive brush biopsy and saliva samples.
Conclusion: Label free optical spectroscopic techniques, such as Raman spectroscopy, can detect biochemical changes underlying cancer progression and could have a future role for identification and monitoring of OPMD.

Application of machine learning algorithms in predicting survival of patients with oral tongue squamous cell carcinoma

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Purpose: The objective was the development and evaluation of 4 ML survival models to stratify patients with OTSCC to predict DSS

Method: Clinic-pathological data were retrospectively collected for a total of 21 features. CPH, RSF, GBS, and SSVM were tested.

Results: The 21 features included some unique pathological variables investigated by our group, such as Tumour-associated tissue eosinophilia, immune-phenotype, tumour budding, and tumour-stroma ratio. SSVM outperformed the other models (C-index=0.69) and high-risk group showed a Hazard Ratio of 4.4 (95%C.I. 2.9 – 7.0, p-value<0.0001) for DSS.

Conclusions: These preliminary results showed that ML algorithms are capable to integrate clinic-pathological variables by accounting of each patient singular features, which are often not considered in routine statistical analysis. ML algorithms might be useful tools to highlight patient's characteristics which are not nowadays included in current TNM staging system, leading to improvements. We believe that definition of standardized analysis flow are required to improve replicability and optimization of results.

Intralesional immunotherapy for the prevention of malignant transformation in high-risk oral potentially malignant disorders

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Purpose: To prevent OPMD risk of malignant transformation by a short course of intralesional immunotherapy

Method: This is a phase II, single arm, proof of concept, multicenter trial.

Results: This is a phase II, single arm, proof of concept, multicenter trial. We will enroll patients (pts) with an histological diagnosis of high risk OPMDs, defined as multifocal (≥2); or contiguous lesions of ≥ 3 cm; or a single lesion ≥ 4 cm or greater in largest diameter with at least 1 lesion with epithelial dysplasia (any degree); or OPMD with 4-quadrant oral cavity involvement (any grade of dysplasia); or OPMD in at least one lesion with moderate dysplasia. Pts will receive 4 cycles of intralesional CD40 agonist mitazalimab 200 mcg/kg, every 2 weeks. After 6 months since treatment start patients will undergo OPMDs resection or biopsy.
Patients with lichen planus or previous immunotherapy are not allowed. The primary objective is the best overall response (complete response + partial response rate) at 6 months, as defined by the percent change in clinical-pathologic composite score. Secondary objectives are safety, risk of malignant transformation, change in histological grade, and quality of life. As exploratory objectives we'll evaluate the presence of prognostic/predictive biomarkers on tissue, blood, and saliva samples. Using an exact binomial test, we require 28 patients to detect activity of study treatment based on a one-sided alpha of 0.1 with 80% power.

Conclusions: An intralesional short course injection of CD-40 agonist may increase killing of OPMDs cells by the activation of the immune system; moreover, it will maximize drug concentration on specific lesions by lowering the risk of systemic toxicities.

Abstracts selected for poster presentation

Poster session view 1 (10:45 am - 11:00 am)

Poster #1 to Poster #18

Poster session view 2 (15:30 to 16:00)

Poster #19 to Poster #37

#1

Global and European Union oral cancer characterization from Global Burden of Disease 2019 – what data show us?

Marta Clemente 1, Carina Ladeira 2

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Purpose: Characterize the incidence and risk factors associated with oral cancer at a global and European level according with GBD 2019.

Method: Data on the burden were obtained from the online data source Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org)

Results: At the global level, the global age-standardized incidence rate (ASIR) of oral cancer increased slightly from 4.28/100,000 to 4.52/100,000 from 1990 to 2019. At EU, from the same period, there was an impressive decrease on the incidence of oral cancer in France, Slovakia, Hungary, and Spain. Notably, a higher prevalence of this cancer is observed among men compared to women, both globally and within the EU. Established risk factors include tobacco use, alcohol consumption, betel quid consumption, and HPV infection, with tobacco being globally significant and alcohol notable in the EU.

Conclusions: The early detection of oral cancer led to reduced aggressive treatment and improved quality of life and overall survival. An organized, population-based oral cancer screening program targeting high-risk groups can reduce mortality in patients with stage III or IV oral cancers. Due to the high cost associated with advanced oral cancer, governments should allocate resources and policy support to the early diagnosis of oral cancer for them to be able to minimize the burden on the country, health care system, and household. Interestingly, artificial intelligence (AI) plays an important role in the early diagnosis in oral cancer, independent of the experience of dentists and public awareness of oral cancer.

#2

Years of Life Lost (YLL) from oral cancer in Portugal in 2019

Carina Ladeira 1, Carla Martins 2

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Purpose: Characterize the Years od Life Lost in the Portuguese population in 2019 due to oral cavity cancer.

Method: Calculation of YLL from the National Oncological Registry (RON) by age and sex.

Results: A total of 22.311,3 YLL were estimated for neoplasms of lip, oral cavity and pharynx for both sexes in 2019, with the oropharynx cancer (4448.8), the hypopharynx (4153.78), and the tongue (3970.72) ranking in the first positions, respectively. The distribution of YLLs ranking by neoplasm is identical to the general population in males, but for females it followed a different pattern: mouth (855.12), tongue (776.49) and salivary glans (421.10) occupied the first positions. % YLL/% mortality ratio ranged from 0.71 to 1.14. Population burden of cancers of tonsils, oropharynx, nasopharynx and hypopharynx is higher than % mortality.

Conclusions: Oral cancers are associated with significant morbidity and mortality, and a profound impact on a patient's quality of life with significant functional, social and aesthetic sequelae. Cancer mortality data are especially important to monitor the effects of screening programs or identify public health prioritization necessities. National programs for oral cancers should also be implemented to reduce mortality and improve patients' quality of life.

#3

Prevalence of OPMDs and OSCCs in the Republic of North Macedonia in a 30-year-period: an analysis based on the data from a single center

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Purpose: To assess the prevalence of oral potentially malignant disorders (OPMDs) and oral squamous cell carcinomas (OSCCs) in patients referred to the Institute of Pathological Anatomy, Faculty of Medicine – Skopje, from the Department of Maxillofacial Surgery and the Department of Oral Surgery, Faculty of Dentistry – Skopje. Ss. Cyril and Methodius University in Skopje.

Method: An electronic database from 1994-2024, which included 17.223 cases from the Institute of Pathological Anatomy was analyzed to determine the prevalence of OPMDs and OSCCs. The following clinical entities were included: leukoplakia, erythroplakia, lichen planus, actinic cheilitis and oral squamous cell carcinoma. The results are shown in frequencies and percentages.

Results: After selection of OPMDs and OSCCs from the database, 2437 cases were included [1500 male (61.5%) and 937 female (38.5%)]. The male to female ratio was 1.6:1. The average age of the patients was 63.83±12.65, with the youngest patient being 17 and the oldest patient being 98 years old. According to the histopathological features, there were 53 cases of leukoplakia (2.2%), 29 cases of oral lichen planus (1.2%), 93 cases of actinic cheilitis (3.8%), 7 cases of oral erythroplakia (0.3%) and 2255 cases of oral squamous cell carcinoma (92.5%). The frequencies and percentages of the affected sites are the following: lips 1109 cases (45.5%), tongue 525 cases (25.8%), floor of the mouth 250 cases (12.3%), mandibular mucosa 247 cases (12.1%), maxillary mucosa 95 cases (4.6%), buccal mucosa 84 cases (4.1%), gingiva 72 cases (3.5%) and palate 55 cases (2.7%).

Conclusion: The most frequently affected sites with OPMDs and OSCCs were the lips and tongue. The significant number of OSCC cases compared to OPMDs underscores the urgent need for heightened awareness and preventive measures against oral cancer in North Macedonia.

#4

Oral cancer prevention and oral mucosal examination among dentists in Norway – a cross-sectional study

Lohar DT1,2,3, Bhattarai BP4, Johannessen AC1,5, Costea DE1,2,5

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2. Center for Cancer Biomarkers CCBIO, Department of Clinical Medicine, University of Bergen
3. Center for International Health, Department of Global Public Health and Primary Care, University of Bergen
4. Institute for Oral Biology, Faculty of Dentistry, University of Oslo
5. Department of Pathology, Haukeland University Hospital, Bergen

Presenter's email: daniela.costea@uib.no

Purpose: To investigate knowledge, attitudes and practices related to oral cancer prevention among dentists in Norway.

Method: Cross-sectional survey based on an electronically administered questionnaire.

Results: The overall response rate was 23.7%. Erythroplakia (83.2%) and leukoplakia (80.4%) were identified correctly by most of the participants in the study as the most prevalent lesions with malignant potential. "Small, painless, indurated ulceration" was identified by 73.6% of the participants, while other common clinical presentations, such as "small, painless white or/and red area" were correctly listed by only 31.4% and 46.4% respectively. Most of participants reported giving counselling to their patients regarding tobacco cessation, while giving counselling regarding excessive alcohol use was not so common. The most common listed barriers to performing oral mucosal examination were reported to be lack of training and/or experience.

Conclusion: Results from the current study highlight strengths as well as gaps in Norwegian dentists' knowledge and practices related to oral cancer prevention and mucosal examination. Data from this study can be used as foundation to reinforce dental curriculum in order to enhance dentists' awareness and knowledge related to oral cancer prevention.

#5

Can we predict the recurrence of oral leukoplakia?

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Purpose: The management of oral leukoplakia (OL) is challenging because of the high risk for recurrence and malignant transformation of OL. Importantly, the recurrent OL are associated with a significantly higher risk of malignant transformation. The present study aimed to examine the association between OL recurrence and various surgical management techniques for OL as well as their clinicopathological factors.

Methods: Electronic searches were performed in a number of databases including Embase, PubMed, Scopus, and Web of Science to retrieve relevant studies. The pooled proportion of OL recurrence after surgical excision was estimated. Subgroup analyses for OL recurrence were performed using the following variables: surgical technique, grades of epithelial dysplasia, anatomical subsites, clinical type and size of the lesion, surgical margin, risk habits, age, sex, and follow-up duration. Additionally, the risk of malignant transformation based on the recurrence status was also estimated.

Results: Eighty studies with a total of 7614 OL samples and various surgical modalities (laser-based techniques, conventional scalpel surgery, cryosurgery, and photodynamic therapy) were included in the current study. A pooled proportion of recurrence of 22% was found. Laser-based surgical methods resulted in fewer OL recurrences than other surgical modalities. OL in the retromolar area and multiple sites, non-homogeneous OL, advanced age, female sex, inadequate surgical margin, retrospective data, and betel quid chewing habits were significantly associated with higher OL recurrence. Of note, recurrent OL were found to have 7.39 times higher risk for malignant transformation than non-recurrent OL.

Conclusions: These results suggest that the combination of laser excision and vaporization might reduce OL recurrence. Furthermore, OL in older patients, females, and non-homogeneous OL need close monitoring after any surgical therapy. Importantly, the recurrent OL lesions require high attention because of their high risk for malignant transformation.

#6

Evaluating the role of a DNA methylation reader, MBD2, in development and progression of HNC

IZGE SHANLITOURK 1, Katerina Strati 1

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Purpose: We propose to investigate the role of a DNA methylation reader, MBD2, in progressive HNC and explore its therapeutic potential.

Methods: We will use an in vitro cell culture model system for progressive HNC and perform RNA-seq and ChIP-seq when MBD2 is knocked-down

Results: Preliminary work from our lab has recently demonstrated a critical role for MBD2 in the transcriptional control of cellular plasticity-related transcription factor Oct4 in the cervix. Our preliminary data identified the DNA methylation reader MBD2 as a potential target for a subset of HNC, which are suggesting that MBD2 knockdown reduces clonogenic abilities of HPV-negative HNC cell lines and inhibits EMT and cell migration in vitro.

Conclusions: Our project aims to further increase the mechanistic understanding of HNC and collectively contribute to the development of novel and non-invasive diagnostics for HNC. Extracting this information will assist us to produce more targeted therapeutic possibilities based on HPV status as well as diagnosing HNC in its early stages.

#7

Preliminary results, perspectives and pitfalls of an automated image analysis approach in oral squamous cell carcinoma (OSCC)

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Purpose : Until now, no image segmentation algorithm has been available to accurately distinguish between various tissue compartments in OSCC. Several researchers have explored deep learning models aimed at distinguishing digitized OSCC histopathological images from non-cancerous tissue through classification tasks, yielding promising results. We propose an approach wherein image analysis focuses on extracting morphological features not readily discernible to the pathologists´ eye with the potential of integration with a systems biology approach, aiming to enhance our understanding of OSCC and pave the way to a personalized oncological therapy.

Method : Using a semi-automated method described by Csűry et al. (2023), we manually annotated 100 OSCC whole slide images (WSIs) from the patient collective of the Otolaryngology Department at the University Hospital Erlangen, along with 44 OSCC WSIs from Centre Léon Bérard (CLB). We trained a U-net-based automated image segmentation model on the Erlangen dataset to recognize the tumor tissue compartment. We applied our model to the CLB dataset and conducted a qualitative and quantitative evaluation of both segmentation approaches.

Results : The semi-automated tissue segmentation required significant time investment for manual annotation. While it achieved a satisfactory level of agreement with pathologist's estimates of tissue composition, it exhibited limited generalizability across WSIs. Nonetheless, this approach served as a stepping stone towards developing the automated segmentation method. The automated segmentation model demonstrated outstanding capability in recognizing tumor tissue, overcoming challenges such as heterogeneity within the tumor tissue, staining variability, diverse staining protocols, and tissue processing artifacts.

Conclusions : Advanced image analysis techniques empower the extraction of in-depth morphological features from OSCC. By integrating these findings with a systems biology approach, the development of mixed-input models becomes feasible, offering further insights into the study of OSCC. Similar strategies may also be applicable in earlier stages of oral tumorigenesis, in particular in patients with oral potentially malignant disorders who may harbor hyperplasia and/or various degrees of dysplasia. This work was in part funded by the INTERCEPTOR Action (CA21140) through a Short-Term Scientific Mission.

#8

Oral lichen planus- an oral potentially malignant disorder of the oral cavity

Ivasiuc Irina 1, Uncuta Andrei 2, Diana Uncuta 1

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2. *"Timofei Mosneaga" Republican Clinical Hospital*

Presenter's email : diana.uncuta@usmf.md

Purpose : The analysis and synthesis of contemporary literature will allow for an overview and update on the etiology of OLP

Method : A bibliographic search was carried out in databases such as PubMed, Hinari, SpringerLink, National Center of Biotechnology .

Results : Oral lichen planus is a chronic inflammatory condition mediated by T-cells in response to various extrinsic antigens, modified autoantigens, or superantigens, with periods of remission and relapse and the potential for malignant transformation.

Conclusions : Oral lichen planus is a chronic inflammatory condition mediated by T-cells in response to various extrinsic antigens, modified autoantigens, or superantigens, with periods of remission and relapse and the potential for malignant transformation.

#9

AI in oral cancer detection: the need for a capability set to guide patient engagement

Brenda Bogaert 1

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Purpose : The purpose of this presentation or poster will be to propose a capability set to guide use of AI technologies

Method : Use of the capabilities approach to conceptualise what kinds of ressources and opportunities patients need to use AI

Results : We propose the following capability set (defined as the resources and opportunities that persons will need to be able to mobillize in their enivornment to effectively understand the use technologies to benefit their health):

1. Access to digital tools, including the ressources necessary to understand and access them
2. Sufficient digital literacy to be able to navigate them
3. Sufficent health literacy to be able to understand, use and appropriate their health knowledge
4. Comprehension of the technology and its uses, including their ability to disengage should they wish and erase health data

Conclusions : Through the capability set, we determine a number of necessary conditions that patients will need in order to use and understand preventive tools for oral cancer, and in particular AI. We believe this capability set can help guide patient engagement and health policy in a person-centered perspective to determine what they will need to be supported in the effective use of technology, including guarding against behavioral changes which may have negative effects (such as avoiding visiting the dentist due to a negative result of the algorithm).

#10

Evaluation of HPV presence in Oral Potentially Malignant Disorders (OPMD) through HPV-DNA/mRNA testing: a multicentric study

Gennaro Musella 1, Vito Carlo Alberto Caponio 1

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Presenter's email : gennaro.musella@unifg.it

Purpose : The purpose of this presentation or poster will be to propose a capability set to guide use of AI technologies

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Conclusions : Through the capability set, we determine a number of necessary conditions that patients will need in order to use and understand preventive tools for oral cancer, and in particular AI. We believe this capability set can help guide patient engagement and health policy in a person-centered perspective to determine what they will need to be supported in the effective use of technology, including guarding against behavioral changes which may have negative effects (such as avoiding visiting the dentist due to a negative result of the algorithm).

#11

Exploring the dynamics of fibroblast heterogeneity in the evolution of oral cancer

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Purpose: Oral squamous cell carcinomas (OSCC) are characterised by a reactive stroma, which is beginning to be described. Cancer-associated fibroblasts (CAFs) heterogeneity in the tumor microenvironment (TME) influences cancer progression and therapeutic responses. Little is known about the evolution of this cell population during the malignant transformation toward OSCC. Our study aims to elucidate the multifaced heterogeneity and role of fibroblasts in shaping TME dynamics and interactions with neighbouring cell types across multiple stages of oral premalignant lesions leading to oral cancers.

Method: We employed advanced single-cell RNA sequencing (scRNAseq) approach (10x Genomix) to analyze HPV-negative OSCC tumor biopsies from 11 treatment naïve patients and one biopsy of oral leucoplakia. Gene set enrichment analysis (GSEA) of gene signatures from CAF subsets was applied to bulk RNA-seq data from a publicly available dataset (GSE227919). 42/66 samples were carefully selected to include normal oral mucosa (n=9), leucoplakia with hyperkeratosis (n=14) or dysplasia (n=10) and OSCC (n=9).

Results: Subclustering of 6234 CAFs from OSCC patients revealed 8 subsets including myofibroblastic CAFs (myCAF), inflammatory CAFs (iCAFs) and one cluster of "Detox" iCAFs, defined based on breast cancer CAF signatures. The heterogeneity of CAFs from OSCC was not fully recovered in the analysis of 1109 CAFs from leukoplakia. Strikingly, iCAF clusters were virtually absent whereas myCAFs and "Detox" iCAF were prominent. CAFs were enriched for both the "Detox-iCAF" and "early-activated CAF" signatures, which partially overlap. On the validation cohort, GSEA revealed that the expression of activated-CAF-specific genes, e.g ecm-myCAF, TGF□-myCAF, and wound-myCAF, was enriched from the leucoplakia stage with a peak in the presence of dysplasia, compared to normal tissue. Although these results need to be confirmed on additional samples and larger cohorts, they suggest that CAFs from oral potentially malignant disorders (OPMD) have a transient phenotype between normal fibroblasts and tumor CAFs.

Conclusions: Our current project delves into the intricate landscape of fibroblast heterogeneity through different stages of oral malignant progression. By delineating evolutionary trajectories of fibroblast heterogeneity, this study will offer insights into fundamental principles governing fibroblasts in OSCC biology and open avenues for interception of OPMD and therapeutic interventions targeting fibroblast-mediated pathologies.

#12

Factors influencing salivary lactate dehydrogenase levels in oral cancer and oral potentially malignant disorders.

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Purpose: To evaluate whether salivary Lactate Dehydrogenase (LDH) levels are higher in patients with OPMD and oral cancer (OC) patients.

Method: Case-control study. LDH in unstimulated saliva was measured. Epidemiological and periodontal variables were collected.

Results: We included 92 patients: 12 patients with OSCC, 51 patients with OPMDs (17 patients with Oral Leukoplakia (OL) and 34 patients with Oral Lichen Planus (OLP)) and 29 control patients (CG). Patients in the groups were similar in sex, age, smoking and alcoholic habits, and UWS flow rate (ml/min). When periodontal variables were compared between the three groups (OSCC, OPMDs and CG), significant differences were observed. Periodontal probing depth (PPD) and Bleeding on probing (BOP) were higher in the OSCC group. However, the Plaque index (PI) was higher in patients with OPMDs. LDH values were higher in the OSCC group than in the OPMD and CG groups. LDH values were in turn higher in the OPMDs group than in the CG. However, no significant differences were observed among the three groups. Also, no differences were observed among the groups when the OPMDs were separated into OLP and OL. When analyzing how the variables collected in the total group influenced salivary LDH values, it was observed that the linear regression model for salivary LDH included group of patients (OSCC, OLP, OL, CG), tobacco (yes, no), sex (male/female), age, UWS flow rate, PPD, and BOP. Only PPD was a significant predictor of LDH. A higher PPD was associated with a higher LDH value (p=0.001). The next variable to contribute to the prediction was age but it was not significant.

Conclusions: The present study cannot confirm, as previous studies in Asia, that LDH values are higher in OC patients than in OPMD and CG patients. Further studies are needed to confirm these results. It is necessary to consider the periodontal status of patients in future studies.

#13

Multi-Institutional Collaboration to optimize OPMD and oral cancer Diagnosis through Machine Learning and Infrared Imaging

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Purpose: Histopathological image analysis remains the gold standard for diagnosing suspected oral cancer or oral potentially malignant disorder (OPMD). This analysis is performed using hematoxylin and eosin (H&E) stained tissue sections that allows to reveal morphological and structural cellular changes. However, it offers limited insights into the underlying cellular processes. Infrared (IR) imaging has emerged as a supporting tool enabling deeper understanding than traditional morphological analysis, providing biochemical compositions. The relationship between morphological and biochemical interactions can be carried out by machine learning (ML) algorithms which can capture the complexity and non-linear interactions. These models rely on learning complex patterns using large amounts of data and requiring sometimes specific acquisition protocols that can be time-consuming, limiting its use in clinical applications. Here, we propose a collaborative, multidisciplinary ML workflow involving four distinct institutions. This collaboration aims to achieve two key objectives. First, we will take advantage of current available data to reduce time required for data acquisition. Second, we will study the benefits of infrared imaging to understand the underlying biochemical composition of OPMDs.

Method: Pre-annotated H&E images from the University Hospital Erlangen will first train a segmentation ML model with the expertise of specialists from Gipsa-lab. Next, the model's predictions will be validated by CLB pathologists on a new dataset containing IR biochemical information acquired using ADMIR's spectrometer. Finally, this new enriched data will be used to fine-tune the ML model, generating more fine-grained predictions while improving model performance.

Expected Results: The main objective of study will be to achieve an image segmentation algorithm based on both morphological and biochemical features by a collaborative work. A similar approach is expected to be applied in OPMD. Whether IR features provide any additional prognostic information as compared with classical histopathological assessment for patients with oral cancer or OPMD will be evaluated.

#14

Referral Patterns for Amalgam-Induced Oral Lichenoid Reactions: An Observational Study

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Purpose: To determine the referral frequency by general dentists of patients exhibiting amalgam-induced oral medicine specialists.

Method: Data were gathered over a twelve-month period.

Results: 72 patients diagnosed with oral lichenoid lesions in contact with amalgam fillings were included in the study. These lesions resolved following amalgam replacement and, where necessary, topical corticosteroid therapy. Patients were categorized into three groups based on their referral pathways: those referred by the general dentist, those who self-identified the oral lesion and sought specialist care, and those diagnosed incidentally by an oral medicine specialist during a routine dental examination. Out of the 72 patients, a substantial majority (75% or 54 patients) were referred by their general dentists. A smaller percentage (16.7% or 12 patients) self-referred after noticing symptomatic changes, while only a few (8.3% or 6 patients) were identified by specialists during routine dental checks.

Conclusions: The study underscores the pivotal role of general dentists in the early detection and referral of patients with amalgam-induced oral lichenoid reactions. General dentists should be able to recognize common oral lesions, as simple procedures such as replacing amalgam fillings can lead to the reduction or resolution of OPMD changes. Although most cases are being referred appropriately, the findings indicate a need for enhanced patient education and improved diagnostic protocols within general dental practices experiencing these reactions, optimizing outcomes and patient well-being in oral medicine.

#15

Tobacco use and prevalence of oral premalignant lesions, among Malayali tribes, Yelagiri Hills, Tamil Nadu, India.

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Purpose: The present study was conducted to assess the tobacco use and prevalence of precancerous lesions and oral cancer among Malayali tribes, Yelagiri Hills, Tamil nadu, India.

Method: The inhabitants of the 14 villages of the Yelagiri hills, who have completed 18years and residing for more than 15years present on the day of examination and who were willing to participate in the study were included. Data was collected from a cross-sectional survey, using a Survey Proforma, clinical examination and a pre-tested questionnaire. An intra-oral examination was carried out by a single examiner using WHO Oral Health Surveys – Basic Methods Proforma (1997).

Results: The overall prevalence of smokeless and smoking tobacco was 78.8% and 65.2% respectively among 1550 study population. Of those who had the habit of smoking, 26% smoked beedi, 10.9% smoked cigarette, 65% chewed raw tobacco, 18% chewed Hans and 28% had a combination of smoking and smokeless tobacco usage. Around 49.8% of samples were stained positive for precancerous and cancerous lesions of the oral cavity. The highest number of positive samples were from buccal mucosa with 46.2% subjects and 12% for labial mucosa. The reason for practicing these habits were as a measure to combat the cold, relieving stress and body pain after work, and the lack of awareness of the hazards of the materials used. Prevalence of oral mucosal lesions in the study population was due to tobacco usage and alcohol consumption and lack of awareness regarding the deleterious effects of the products used.

Conclusions: Oral cancer is highly prevalent in this Malayali tribes owing to high tobacco consumption rates and habits warranting the cessation center a priority. Also, early detection and screening are vital to attaining better outcomes.

Increasing access to available phenotypic characterization of OPMD in the public domain (OPMDxpress)

#16

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Purpose: Natural history of oral potentially malignant disorders (OPMD) is poorly understood. Understanding the underlying driving biology leading to transformation is of paramount importance to improve early detection and develop rationally-based interventions for interception. Mining transcriptomic data represent a classical approach to interrogate the biological mechanism involved during tumorigenesis. Over the last 20 years, with the development of high-throughput technologies (array-based and now NGS-based), most research groups have made their data available to the scientific community. However, this data is scattered in several repositories, datasets annotation is unsystematic, and metadata has not been curated, thus limiting accessibility and reusability to the scientific community. In order to address those challenges, within the context of INTERCEPTOR COST Action, we propose to lead an effort that will involve a group of (young) investigators of different backgrounds (biological, clinical, data science, bioinformatics, histopathological…) across Europe, to systematically map available data in public repositories, describe them (technology, raw data availability, available format), curate available metadata and disseminate the information to the INTERCPETOR community and beyond. This will include studies involving OPMD and whenever available normal mucosa and oral cancer.

Method: We propose the following milestones: initiative presentation at the 3rd OPMDay and call for interest (June 2024), definition of the search strategy (July 2024), literature and public repositories search (August-November 2024); presentation at a Core group meeting to get feed-back (December 2024); datasets description and metadata curation (January-April 2025); presentation at the 4th OPMDay. Combine a set of standardized annotated OPMD datasets along with their clinical and histopathological description that will be easily accessible to all members of INTERCEPTOR Action and beyond.

Expected results: OPMDxpress is relevant to WG1 (Data science and medical informatics to understand OPMD trajectory) and WG4 (Preclinical and clinical research for the development of innovative preventive strategies). We believe this effort will foster collaboration within the network and facilitate translational research. Finally, it is in line with the FAIR principles for scientific data management by facilitating findability, accessibility, interoperability and reuse of data.
The overall prevalence of smokeless and smoking tobacco was 78.8% and 65.2% respectively among 1550 study population. Of those who had the habit of smoking, 26% smoked beedi, 10.9% smoked cigarette, 65% chewed raw tobacco, 18% chewed Hans and 28% had a combination of smoking and smokeless tobacco usage. Around 49.8% of samples were stained positive for precancerous and cancerous lesions of the oral cavity. The highest number of positive samples were from buccal mucosa with 46.2% subjects and 12% for labial mucosa. The reason for practicing these habits were as a measure to combat the cold, relieving stress and body pain after work, and the lack of awareness of the hazards of the materials used. Prevalence of oral mucosal lesions in the study population was due to tobacco usage and alcohol consumption and lack of awareness regarding the deleterious effects of the products used.

#17

Malignant Transformation of Oral Lichen Planus in non-smokers and non-alcohol users: a case series

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Purpose: To describe the mean features of 5 patients affected by oral lichen planus (OLP) who developed OSCC during the last year.

Method: Patients affected by OLP underwent periodic follow-up visits at the Oral Medicine Unit "V. Margiotta" of Palermo (Italy).

Results: During follow-up visits, patients who presented clinically suspicious signs of malignant transformation underwent a biopsy. In 5 cases, the diagnosis of OSCC was performed. So, data from included patients affected by OLP without any remark of epithelial dysplasia who developed OSCC in the last year were collected: 3 were males (3/5; 60%) and 2 females (2/5; 40%), with a mean age of 71.4 ± 9.5 years. All patients presented multiple lesions in the oral cavity at the first visit. The tongue was the most frequently biopsied site (3/5; 60%), followed by masticatory mucosa (1/5; 20%) and buccal mucosa (1/5; 20%). All included patients developed OSCC at the same anatomical site where the biopsy was previously conducted for OLP diagnosis. The mean time between the first OLP diagnosis to OSCC development was 22 months in the tongue, 24 months in the masticatory mucosa, and 40 months in the buccal mucosa. None of the patients were smokers or alcohol users.

Conclusions: The tongue is the most affected site by OSCC, also in our series with a prior diagnosis of OLP without dysplasia. Moreover, when OLP is localized on the tongue, malignant transformation occurs more rapidly. These findings underscore the importance of follow-up visits in OLP patients with particular attention to this anatomical site to intercept any early signs and promote early diagnosis of OSCC.

#18

Buccal micronucleus cytome assay in human oral cancers

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Purpose: We applied MN test in exfoliated buccal cells to study genetic instability in cancer patients in Armenia for the first time.

Method: MN test has been applied to oral mucosa cells among oral cancers, considering them as targets for carcinogens.

Results: We applied MN test in exfoliated buccal cells to study genetic instatbility in cancer patients in Armenia for the first time. In our study, buccal cells from 20 patients with cancer, as well as from 20 healthy individuals (control group), were assessed for the presence of MN and other nuclear anomalies reflecting cytotoxic effects.
We found significantly increased frequencies of MN in patients with cancer compared to the control group. The average ratio (MN in patients / MN in control group) was 4.1. The frequencies of all other nuclear anomalies were also significantly elevated in all patients compared to the control group.

Conclusions: Our preliminary data show a significantly elevated level of MN and other nuclear anomalies in cancer patients compared to healthy individuals. Micronuclei (MN) are formed due to structural and numerical chromosomal aberrations. Measuring MN in human cells has become one of the most widely used methods to measure chromosome instability and the damaging effects on DNA of environmental exposures and endogenous genotoxic agents.

#19

DOES THE NEUTROPHIL/LYMPHOCYTE INDEX HAVE PROGNOSTIC VALUE IN SEVERITY IN ORAL LICHEN PLANUS?

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Purpose: Oral lichen planus (OLP) is a potentially malignant disorder, a chronic inflammatory condition of an immune nature. The aim of this study is to investigate the association between immune-inflammatory biomarkers in patients with OLP and the control group.

Method: Retrospective case-control study with 129 patients (62 with OLP and 67 controls) in which clinical and laboratory data were analyzed. The neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), as well as the mean platelet volume (MPV) index and the parameter systemic immune-inflammation index (SII) were assessed.

Results: In OLP patients the average time of progression was significantly longer when the condition manifested in the atrophic-erosive form (4.3±3.2 years) versus the reticular form (1.8±0.9 years) ($p = 0.018$). With regard to NLR no differences were found in terms of age ($p = 0.346$) ($r = 0.08$), tobacco use $p= 0.807$, sex ($p = 0.088$), alcohol consumption ($p = 0.281$), clinical form of OLP ($p = 0.55$), time of progression of OLP ($p = 0.309$)($r = -0.13$) and number of sites ($p = 0.217$). The same occurs regarding the systemic immune-inflammation index.

Conclusions: The lack of significant statistical association in the biomarkers and parameters (NLR, PLR, MPV and SII index) in patients with oral lichen planus makes such parameters of very limited use in the clinical practice of OLP.

#20

miRNAs signatures in oral Leukoplakia and oral Lichen Planus

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Purpose: To identify expression of miR-29a, miR-34b in oral leukoplakia(OL) and miR-4484, miR-155, miR-146a in oral Lichen Planus(OLP).

Method: Serum&Saliva quantification with PCR, mRNAs expression measured by TRIzol Kit and gene expression assessed by Real time PCR.

Results: The expression data was used for cluster analysis of normal and diseased tissues. qPCR analysis showed down regulation (decrease expression) of serum and salivary miRNAs (29a, 34b, and 423) in oral leukoplakia compare to control group (p value less than 0.001). The serum and salivary level of miR-4484, miR-155, miR-146a, and miR-21 in oral lichen planus showed significantly up-regulated (increased expression) compared to control. (p value less than 0.001.)

Conclusions: miRNA genomics can be used as molecular biomarkers in early diagnosis, therapeutic and prediction of conversion potential of oral lichen planus and oral leukoplakia in oral cancer. Follow up studies evaluating miRNA signature in oral lichen planus by sequential sampling will aid in validating our hypothesis. Further, establishing such miRNA signature databases may serve as therapeutic targets in future.

#21

Lysyl Oxidase Gene in Pathogenesis and Malignant Transformation of Oral Submucous Fibrosis

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Purpose: Identification and comparison of gene expression of Lysyl oxidase (LOX) in oral submucous fibrosis and controls and to determine its role in Pathogenesis of Oral submucous fibrosis.

Method: Of total sample size (n=127), the whole blood sample were collected from case and control group in citrate vial. It is centrifused and stored at -800C. We collected and isolated RNA from blood of case group (n=127) and age and sex matched control group (n=127) recruited on the basis of inclusion criteria. The cDNA was prepared for 127 samples which were processed for gene expression of Lysyl oxidase (LOX) in relation to house¬keeping genes (Beta actin and 18srRNA) and its role in pathogenesis of Oral submucous fibrosis.

Results: In relative expression (Normalized ratio),relatively 11 cases shown down-regulation of lysyl oxidase gene while 27 cases shows up-regulation of lysyl oxidase gene while in 89 cases there were no regulation i.e expression of lysyl oxidase gene in case group was of same degree of control. In non-relative expression results (Non-norma¬lized ratio), the 38 cases shown down regulation of LOX gene while in 53 cases, it was up-regulated however in remaining 36 cases there was neither up-regulation nor down-regulation of Lysyl oxidase gene i.e the expression of LOX gene is null.

Conclusions: In oral submucous fibrosis, the expression of Lysyl oxidase gene is mixed type i.e either it will down regulate/upregulate or there will be no expression at all comparatively. However in majority of cases the upregu¬lation of lysyl oxidase is relatively more common than down-regulation or non expression of Lysyl oxidase gene. So the hypothesis till date that lysyl oxidase(LOX) gene is only up-regulted, is overruled.

Key words: Oral Submucous fibrosis, Lysyl oxidase, betel nut, premalignant disorders.

#22

Raman spectroscopy for identification and monitoring of oral potentially malignant disorders

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Purpose: This presentation will discuss our recent and current work on Raman spectroscopy for identification of OPMD.

Method: Raman spectroscopy was used to detect biochemical changes in FFPP tissue, brush biopsies and saliva.

Results: Using FFPP tissue sections, we showed the ability of Raman spectroscopy to discriminate between benign oral lesions and mild, moderate and severe dysplasia. We also showed good discrimination between oral exfoliated cells (brush biopsy) from patients with oral leukoplakia (OLK) and healthy volunteers, differentiation of low (no and mild dysplasia) and high risk (moderate and severe dysplasia) OLK and the detection of field cancerisation. Similarly for saliva samples, we demonstrated discrimination between patients with OLK and healthy volunteers and differentiation between low and high risk OLK. Our current study is focussed on monitoring the progression of OPMD in patients using Raman spectroscopic analysis of minimally invasive brush biopsy and saliva samples.

Conclusions: Label free optical spectroscopic techniques, such as Raman spectroscopy, can detect biochemical changes underlying cancer progression and could have a future role for identification and monitoring of OPMD.

#23

Investigating the effect of sample storage on Raman spectra from oral exfoliated cells and saliva.

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Purpose: To investigate the useability of exfoliated cells and saliva samples after over 5 years of sample storage.

Method: Saliva and exfoliated cell samples previously collected (>5 years) from healthy donors were used in the study.

Results: Raman spectra were recorded from the exfoliated cell samples previously prepared on ThinPrep slides and freshly prepared on new ThinPrep slides (about 25 cells per sample depending upon sample quality) from the stored vial. Raman spectra were recorded from saliva samples previously stored at -80℃. Using Principal Components Analysis, Raman spectra recorded from the stored cell and saliva samples were compared to previously recorded spectra from the same samples prepared at the time of collection to identify any biochemical changes as a result of sample storage.
The Raman spectra show significant changes in both the stored cell and saliva samples, as compared to the same samples prepared at the time of collection. The changes were observed in lipids and protein in the case of cell samples, while evident protein degradation was observed in the case of saliva samples.

Conclusions: Even though cell samples were fixed and saliva was stored at -80 ^{0}C, changes were observed over time. This suggests that long-term storage (>5+ years) of biological samples should be avoided where possible. Further, this study will be extended to understand the effect of storage on patient samples and the development of models for differentiating patient pre-cancer samples from healthy volunteer samples.

#24

THE ROLE OF 18F-FDG PET/CT IN THE DETECTION OF TONSILLAR CANCER AFTER TREATMENT AND CORRELATION WITH CT

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Purpose: Estimation of diagnostic usefulness of 18F-FDG PET/CT in detection of tonsilar cancer after treatment and correlation to CT.

Method: Indications for 18F-FDG PET/CT: post-treatment restaging with positive/uncertain CT, follow-up, suspected recurrence.

Results: Thirty two patients (19 males, 13 females), mean age (54.3±6.7), with tonsillar cancer (15 Non-Hodgkins lymphoma, 12 planocellular cancers, 2 squamocellular cancers, 2 Hodgkins lymphoma and 1 plasocytoma) after tonsillectomy (10 left side, 11 right side and 11 billateral tonsilectomies) and chemo/radiotherapy were investigated. 18F-FDG PET/CT findings were compared to clinical follow-up of up to 10 years after imaging. Degree of metabolic activity was analyzed visually and semi-quantitatively using maximum standardized uptake value (SUVmax). High accumulation of radiopharmaceutical was found in 18 (56.2%) patients who were considered true positive. Recurrence was local in 5 patients with mean SUVmax 14.04, then in neck, mediastinum, lung and pleura, bones. Physiological uptake was found in 12 patients (37.5%) and only two males (6.2%) were false positive. Overall sensitivity of 18F-FDG PET/CT was 100%, specificity 85.7%, positive predictive value 90%, negative predictive value 100% and accuracy 93.7%. In 11 cases (34.3%) PET/CT findings significantly influenced further management of the patients. Pearson Chi-square test showed statistically significant difference between the results of 18F-FDG PET/CT and CT ($P<0.05$).

Conclusions: 18F-FDG PET/CT is a valuable tool for follow-up of tonsillar cancer after treatment due to its high sensitivity, specificity, PPV, NPV and accuracy. It can influence the patients' management in significant number of cases. 18F-FDG PET/CT was superior to CT in evaluation of therapy response, active disease in residual tissue and normal size lymph nodes.

#25

An early cost-effectiveness analysis of a hypothetical prognostic biomarker for risk stratification in OPMD

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Purpose: Investigate the potential cost-effectiveness of a hypothetical biomarker for stratifying patients with OPMD.

Method: The study employs methods of early cost-effectiveness analysis.

Results: These methods provide a preliminary evaluation of the cost-effectiveness of a health technology not yet adopted in clinical practice, to determine the criteria under which the technology would be cost-effective. A decision tree plus a time dependent state transition model is used to model potential pathways of patients from the "standard of care" arm and the "biomarker informed" arm.
Patients' survival, quality of life and treatment costs will be based on literature. The study evaluates various scenarios to determine the efficacy, price, and OPMDs management approach that would render the biomarker cost-effective in the Netherlands, if compared with the standard prognostic procedure.
A value of information analysis is conducted to determine the cost of additional research and to assess the value of obtaining further information on the core biomarker characteristics that have the highest uncertainty.

The study is currently in progress. During the conference, we will present the results of the base case scenario, in terms of both life years and quality-adjusted life years gained. We will also discuss the total costs associated with the new biomarker prognostic approach from the Dutch healthcare system perspective.
Through threshold analysis, we identify the minimum accuracy, associated costs, and expected outcomes that would make the potential biomarker cost-effective.

Conclusions: As the study is ongoing, it's premature to draw any conclusion. It's worth noting that this is the first cost-effectiveness analysis of a biomarker for stratifying OPMDs in a European setting. This highlights the novelty and potential impact of this study.
The outcomes of this analysis are expected to serve as a guidance for future research on the cost-effectiveness of implementing a prognostic biomarker in clinical practice for stratifying patients with OPMDs, for their risk of developing oral squamous cell carcinoma.

#26

Genetic and epigenetic biomarkers in young patients with Oral Squamous Cell Carcinoma: a pilot study

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Purpose: Characterize Juvenile -OSCC's clinical, histopathologic, genetic, and epigenetic profiles to identify early OSCC biomarkers.

Method: Whole Exome Sequencing and DNA methylation analysis will be performed on formalin-fixed paraffin embedded tissue samples.

Results: Previous studies have demonstrated that the J-OSCC is highly aggressive; indeed, younger patients present a high rate of locoregional and distant metastases, suggesting that the early age onset represents an adverse and independent prognostic factor. Relapse occurs sooner and faster, tumor specific survival is shorter. These findings may suggest that J-OSCC had a different genetic profile compared to older patients with the same disease. So far we have collected 20 OSCC samples in patients < 45 years old, and we will soon begin first the Whole Exome Sequencing and then the DNA methylation. Expected findings could include the identification of novel mutations or the confirmation of known mutations (e.g. TP53, HRAS, NOTCH, CDKN2A, PIK3CA) that contribute to the development and progression of OSCC in younger patients.

Conclusions: In conclusion, by thoroughly examining the clinical, histological, genetic, and epigenetic landscape of juvenile OSCC, this pilot project seeks to close a major knowledge gap regarding the onset and progression of the disease in younger individuals. New molecular biomarker discovery for early diagnosis and prognostication of Juvenile OSCC could reform screening protocols and customize treatment procedures, improving patients' quality of life and survival rates.

#27

Accuracy of different large-language models in oral potentially malignant disoderd meta-analysis

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Purpose: Test the accuracy of LLM-based tools in the data extrapolation of studies in oral potentially malignant disorders.

Method: PICO: What is the malignant transformation rate of oral proliferative verrucous leukoplakia?

Results: Using the PICO methodology, ChatPDF, ChatGPT-4, and Elicit were tested and asked to report in a table the number of transformed oral proliferative verrucous leukoplakia and the number of total cases.
The target outcome was the number of transformed cases, and total sample size among the included studies from a oral medicine meta-analysis. All the three platforms employed were able to accurately extract the information required. Agreement was reached, with a K-value of 0.87 among the three platforms. ELICIT performed the less.

Conclusions: While not orginally designed to this purpose, the inclusion of LLM in the SRMA of oral potentially malignant disorders outcomes may represent a reliable tool to improve and speed up data extraction. However, improvements are still required as accuracy did not reach 100% and human supervision is still needed.

#28

Identification of oral cancer-associated microRNAs in aging female mice exposed to lifelong calorie restriction

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Purpose: Identification of oral cancer-associated microRNAs in aging female mice exposed to lifelong calorie restriction.

Method: Blood samples were collected at weeks 49/50, and 81/82 of mouse age. Expression levels of miRNAs were measured using Affymetrix.

Results: Beneficial effects of caloric restriction (CR) in various diseases including cancer, have been reported in the literature in both animal and human studies. Our group is one of the leading groups to study the effects of CR in cancer development. To better understand the molecular mechanisms of the preventive effects of CR in cancer development the roles of various factors including hormones, adipokines and epigenetic modifications have been studied. Yet, there are many questions that remain unanswered. Identifying OC-related epigenetic regulators is crucial for early diagnosis of the disease. In this study, the effects of the two different types of CR on the miRNA expression levels targeting the OC-associated genes were investigated. Mice were enrolled into three different dietary groups: ad-libitum(AL), chronic CR(CCR, 15% restriction), and intermittent CR (ICR) which was applied to three weeks of AL feeding and one week of 60% restriction in cyclic manner. Blood samples were collected at weeks 49/50, and 81/82 of mouse age. Expression levels of miRNAs were measured using Affymetrix GeneChip miRNA 4.1 Array. OC-associated miRNAs reported in at least two independent studies were compared between the dietary groups. At week 50, mmu-miR-18a-5p which was reported to be upregulated in oral cancer was downregulated by 5.5 fold in CCR group compared to the AL group. At week 80, mmu-miR-18a-5p, mmu-miR-24-3p and mmu-miR-31-5p were downregulated by at least 2 fold by ICR type of CR which was reported to be more beneficial for cancer prevention in other types of cancer studies.

Conclusions: These results reveal that CR modulates the OC-related miRNAs which could be good candidates for early diagnosis, prognosis and also be potential therapeutic targets in the fight against oral cancer.

#29

Lack of Gαq at tumor stroma: a driving force in the development of Head and Neck Squamous Cell Carcinoma

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Interactions among different cell types present in the tumor microenvironment play a key role in cancer progression. Head and neck squamous cell carcinomas (HNSCC) are one of the most aggressive types of tumors. Interactions between HNSCC cells and the surrounding stroma seems to be critical in the determining tumor aggressiveness and metastasis. However, the mechanisms underlying these processes remain elusive. Altered expression and activity of G protein-coupled receptors (GPCRs) and of G proteins has been associated with increased tumorigenicity in specific cancer cells, but their role in tumor stroma cells requires further investigations. Fibroblasts, a major component of the stroma, can impact tumor cell features through diverse mechanisms including extracellular matrix remodeling, exosomes release, and altered autophagy. We have recently uncovered Gαq as an essential regulator of the autophagy flux, via a non-canonical effector region capable of interacting with proteins containing PB1 domains.

In this context, we have explored whether modulation of Gαq expression in fibroblasts can impact key features of these cells related to cancer progression and HNSCC cells invasive features. Our results show that the absence of Gαq in murine embryonic fibroblasts drastically induces their activation profile and fosters their pro-tumorigenic capacity through the regulation of tumor stromal composition and architecture. Gαq-KO fibroblasts display aberrant ECM deposition and remodeling favoring the generation of "traffic lanes" around HNSCC tumoral cells that seem to promote its migratory and invasive capacity both in vitro and in vivo. In addition, altered exosome secretion and composition in Gαq-KO fibroblasts appears to have marked effects on HNSCC cells tumoral features.

Overall, our data put forward Gαq as a new player in the HNSCC tumor microenvironment modulation through the control of fibroblast plasticity and functionality, opening the way for novel therapeutic strategies.

#30

Study of uncertainty in patients undergoing screening for potentially malignant oral disorders (PMODs)

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Purpose: Potentially malignant oral disorders (PMODs) represent a major public health challenge, requiring particular vigilance.

Method: To achieve these aims, we opted for a mixed-methods approach combining qualitative interviews with patients diagnosed with OPMD.

Results: The initial results of our study show higher participation by women than men, with cervical, breast, colorectal, lung and skin cancers being the most frequently screened. The reasons for screening are mainly linked to the recommendation of a GP, the presence of a family history of cancer, age, and public campaigns to raise awareness of screening. Most respondents estimate the frequency of screening at less than once a year. Waiting for the results is generally accompanied by a degree of anxiety, shared in particular with the spouse.

Conclusions: We find that uncertainty is an intrinsic component of the OPMD screening process, but that its nature and impact on patients remain poorly understood. Our results highlight the need for a holistic approach to patient management, in order to improve their screening experience and quality of life.

#31

Oral cancer Incidence in Albania, future challenges

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Purpose: This is a retrospective study that aims to gather data from one of the largest Hospital Centers in Albania and update the Cancer Registry of Albania with accurate present data for oral potential malignant disorders. This study will fill in the gap of information about the incidence of oral cancer in Albania and also lead to other possible collaborations in order to increase awareness among dentists or oral hygienists for early detection and prevention of oral cancer. There is need for continuing education regarding early detection and prevention of oral cancers and precancerous lesions in Albania.

Method: This is a retrospective study that is gathering information from the cancer registry of the "Mother Theresa " University Hospital Center in Tirana (TUHC). Patients records were gathered from the Department of Medical Statistics, Medical University of Tirana. Data is being processed by SSP3 program. There are some excluding factors as follows:
1. Cases in witch the diagnosis is not determined yet.
2. Patient records that do not confirm the diagnosis.
3. Patient records that are not fully completed, or miss completed.

This method has some limits. One of the biggest limits is taking into consideration only the public Hospital and leaving outside of the study cases diagnosed in private hospitals or abroad.

Results: This is an ongoing study and we are processing the data gathered from the University Hospital Center in Tirana. The incidence rate of Oral Cancer as reported by the International Agency for Research on Cancer was 1,2% up to 2020.The death rate from oral cancer in Albania has reached 90 or 0,31% of total deaths as reported up to 2020. Albania ranks 138-th globally with a death rate 1,92 per 100.000 population.

Conclusions: Although several efforts to control cancer are underway, oral cancer in Albania is often detected in the later stages. Cost limitations, inadequate technology, and insufficient training of medical personnel for widespread screening measures have severely limited oral cancer screening in Albania. Dentists and dental hygienists should be involved in prevention policies, diagnosis and follow -up in order to create a specific national oral cancer registry as an integrated part of Albanian Cancer Registry.

#32

Bibliometric Analysis and Science Mapping for Oral Cancer: Descriptive Research

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Purpose: This research was conducted to present the studies resulting from bibliometric analyzes on oral cancer published in the field.

Method: The data was obtained from the "Web of Science Core Collection" database on March 2. Analyzes were made with the VOSviewer program.

Results: We included 2117 original studies published between 2015 and 2024. Oral cancer research in dentistry was conducted by 1804 authors and 824 institutions from 70 countries. The most prolific authors in this research area were Simon Roger, Warnakulasuriya and Camile Farah (n=19). The most prolific countries and institutions are India (n=289) and the United States of America (n=282). The journal that accepts the most oral cancer research is Oral Oncology (n=298). The top 5 most used keywords in oral cancer research are oral cancer, oral squamous cell carcinoma, head and neck cancer, squamous cell carcinoma, pronosis. The most cited publication was "Syzygium cumini extract induced reactive oxygen species-mediated apoptosis in human oral squamous carcinoma cells" (n=314).

Conclusions: As a result of our research, it was seen that the research trends and popular points of this field are the keywords oral cancer, oral squamous cell carcinoma, head and neck cancer, squamous cell carcinoma, prognosis and the most studied topics are head and neck cancer, oral lichen planus, flap and dental implants. It is believed that our research results can help researchers, health professionals and institutions to find researchers, countries or institutions with whom they can collaborate.

#33

ULCERATIVE COLITIS AND ORAL SQUAMOUS CELL CARCINOMA: A CASE REPORT

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Purpose: The purpose of this report is to explore the link of ulcerative colitis in the development of oral squamous cell carcinoma.

Method: A case report will be presented of a 38 year old male who presented with a chronic ulcer and erythroleukoplakia of his tongue.

Results: The patient presented with a history of ulcerative colitis and no other traditional risk factors for oral squamous cell carcinoma. Histopathology of two incisional biopsies of the tongue reported moderately differentiated invasive oral squamous cell carcinoma and mild to moderate oral epithelial dysplasia, respectively.

Conclusions: Mechanisms to the potential carcinogenesis in a young male patient, with no traditional risk factors of cigarette smoking and alcohol use, who developed oral squamous cell carcinoma, will be discussed. The primary and secondary mechanisms of ulcerative colitis and its carcinogenic potential will be explored along with field cancerization.

#34

Salivaomics- Rediscovering the future of diagnostics

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Purpose: Scoping review of Salivaomics in OPMD and oral cancer diagnosis.

Method: Literature search using MESH terms OPMD, Salivaomics, OSCC, Diagnosis, in Pubmed, Google Scholar, Scopus.

Results: Work in progress, with articles with genomic, transcriptomic, proteomic, metabolomic, microbiomic and immuno-omic biomarkers under study. Evaluation of these studies, for standardization and collection methods, specificity and sensitivity of biomarkers in diagnostics as well as their cost effectiveness in upscaling and adapting as point of care diagnostics . The idea behind this review is to elucidate existing technologies in saliva diagnostics and re-search for the best solution towards early detection which can be utilized efficiently in low and medium income countries. The purpose of this review is to design a study which can be effectively implemented in low resource setting for screening and early diagnosis of oral cancer, along with identifying the high risk OPMDs, with greater chances of malignant transformation. Searching for the holy grail in the spit, to prevent the high mortality and morbidity associated with oral cancer.

Conclusions: In progress.

#35

Study on patient experience of uncertainty in OPMD detection

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Purpose: Address sociological, anthropological, ethical concerns in OPMD detection for better implementation and patient uncertainty management.

Method: Interviews of 30 people diagnosed with OPMD needs to be carried out to confirm the value of working on the issue of uncertainty.

Results: This study can be expected to lead to better management of at-risk patients, particularly in terms of their experience of uncertainty in its various dimensions. The main innovation of this study will be that the issue of uncertainty has been little developed in the field of sociology and ethics of screening, and not at all in the field of screening or early detection of oral cancers. This has repercussions on care for patients from this vulnerable group, who often suffer from conflictual relationships with healthcare providers due to so-called "bad" health behaviors including consumption of alcohol and tobacco. Clearly, there is a need to better understand their perspectives in order to improve care and screening for this vulnerable group.

Conclusions: This study can be expected to lead to better management of at-risk patients, particularly in terms of their experience of uncertainty in its various dimensions. The main innovation of this study will be that the issue of uncertainty has been little developed in the field of sociology and ethics of screening, and not at all in the field of screening or early detection of oral cancers. This has repercussions on care for patients from this vulnerable group, who often suffer from conflictual relationships with healthcare providers due to so-called "bad" health behaviors including consumption of alcohol and tobacco. Clearly, there is a need to better understand their perspectives in order to improve care and screening for this vulnerable group.

#36

EFFECTS OF TRADITIONAL, ELECTRONIC CIGARETTES AND HEAT-NOT-BURN DEVICES ON THE ORAL CAVITY

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Purpose: Evaluate effects of traditional, electronic cigarettes and heat-not-burn devices on the oral cavity.

Method: Systematic review of the literature.

Results: Traditional cigarettes are the ones that cause most damage to the oral cavity, if they are compared with the other two devices. But electronic cigarettes and heat not burn devices are also not risk-free.

Conclusions: More studies are needed to assess the effects of electronic cigarettes and heat not burn devices on the oral cavity.

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