



The 8th International Electronic Conference on Medicinal Chemistry (ECMC 2022)

01-30 NOVEMBER 2022 | ONLINE

Selected biomarkers of inflammation in patients with head and neck cancer depending on the tumor location

Chaired by **DR. ALFREDO BERZAL-HERRANZ**;
Co-Chaired by **PROF. DR. MARIA EMÍLIA SOUSA**



pharmaceuticals



Jarosław Nuskiewicz^{1,*}, Marlena Budek¹, Jolanta Czuczejko^{2,3}, and Karolina Szewczyk-Golec¹

¹ Department of Medical Biology and Biochemistry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, 24 Karłowicza St, 85-092 Bydgoszcz, Poland;

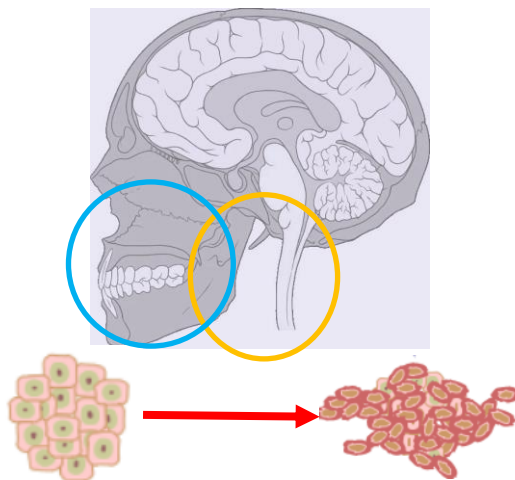
² Department of Psychiatry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Toruń, 9 M. Curie Skłodowskiej St, 85-094 Bydgoszcz, Poland;

³ Department of Nuclear Medicine, Oncology Centre prof. Franciszek Łukaszczyk Memorial Hospital, Bydgoszcz, 2 dr I. Romanowskiej St, 85-796 Bydgoszcz, Poland.

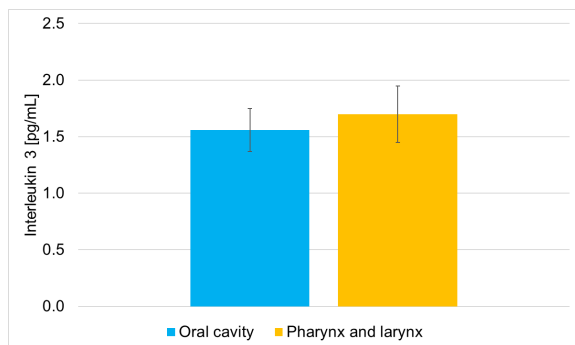
* Corresponding author: jnuskiewicz@cm.umk.pl

Selected biomarkers of inflammation in patients with head and neck cancer depending on the tumor location

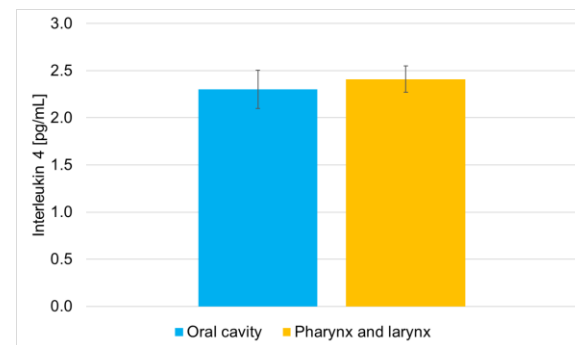
Graphical Abstract



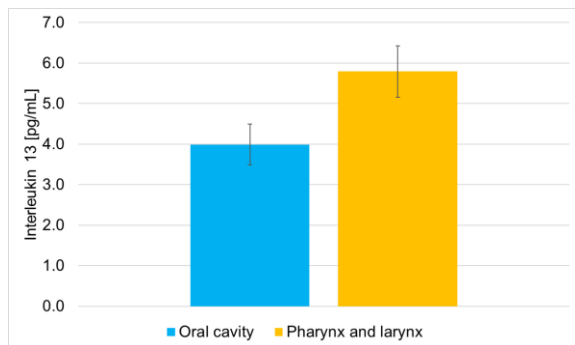
IL-3



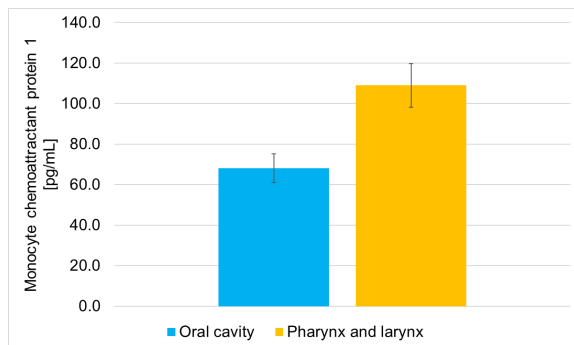
IL-4



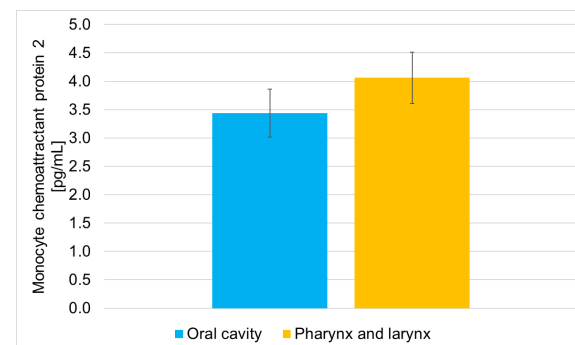
IL-13



MCP-1



MCP-2



Abstract:

Head and neck cancers (HNCs) are a group of neoplasms located in the area of oral cavity, pharynx, larynx, paranasal sinuses, nasal cavity, salivary glands. HNCs are the sixth most common type of cancer in Europe population. As in other neoplastic diseases, chronic inflammation occurs in HNC, affecting not only the location of the tumor, but also distant healthy tissues. In patients with HNC, changes in the levels of pro- and anti-inflammatory cytokines are observed. The aim of the study was to assess the level of interleukin 3 (IL-3), IL-4, IL-13, monocyte chemoattractant protein 1 (MCP-1) and MCP-2 in patients with HNC depending on the tumor localization.

The study group consisted of 40 HNC patients divided into two groups according to the localization of tumor: 20 subjects with cancer located in the area of oral cavity (OC) and 20 subjects with cancer located in the area of pharynx and larynx (PL). Blood serum samples were used to perform analysis. $p < 0.05$ was considered as statistically significant.

In the PL group, statistically significant higher concentrations of IL-13 and MCP-1 were observed. The level of IL-13 in the OC group was 3.99 ± 0.50 pg/mL, while in the PL group it was 5.79 ± 0.64 pg/mL. The MCP-1 concentration was 68.15 ± 7.06 pg/mL and 109.01 ± 10.76 pg/mL, respectively. There were no statistically significant differences in the levels of IL-3, IL-4 and MCP-2. These studies indicate that IL-13 and MCP-1 may be potential biomarkers differentiating tumor localization in patients with HNC.

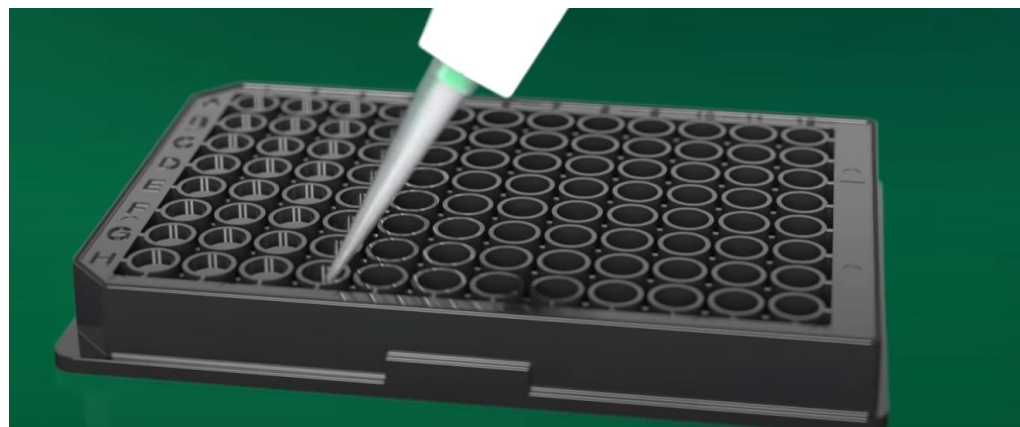
Keywords: biomarkers; cytokines; head and neck cancer; inflammation

Introduction

- Head and neck cancer (HNC) develops from tissues located in the lip, oral cavity, pharynx, larynx, salivary glands, nose cavity, sinuses or the skin of the face.
- HNC is the sixth most common type of cancer in Europe population with more than 150,000 new patients diagnosed every year.
- Approximately 60% of patients with HNC present with locally advanced disease at diagnosis and 60% of people diagnosed at an advanced stage die from the disease within 5 years.
- Alcohol consumption, smoking, human papillomavirus (HPV) and Epstein-Barr virus (EBV) infections are major risk factors for HNC.
- Inflammation is an inherent element of carcinogenesis. It leads to the modulation of the immune system, changing the profile of endogenous pro- and anti-inflammatory factors.
- The aim of the study was to assess the level of interleukin 3 (IL-3), IL-4, IL-13, as well as monocyte chemoattractant protein 1 (MCP-1) and MCP-2 in patients with HNC depending on the tumor localization.

Introduction – materials and methods

- The study group consisted of 40 patients with HNC divided into two groups according to the localization of the tumor.
- Blood serum samples were obtained after collecting venous blood specimens.
- Interleukin 3 (IL-3), IL-4, IL-13, monocyte chemoattractant protein 1 (MCP-1) and MCP-2 levels were determined using the Bio-Plex Multiplex Immunoassay System Bio-Rad.
- The results were presented as means \pm SEM.
- $p < 0.05$ was considered as statistically significant.

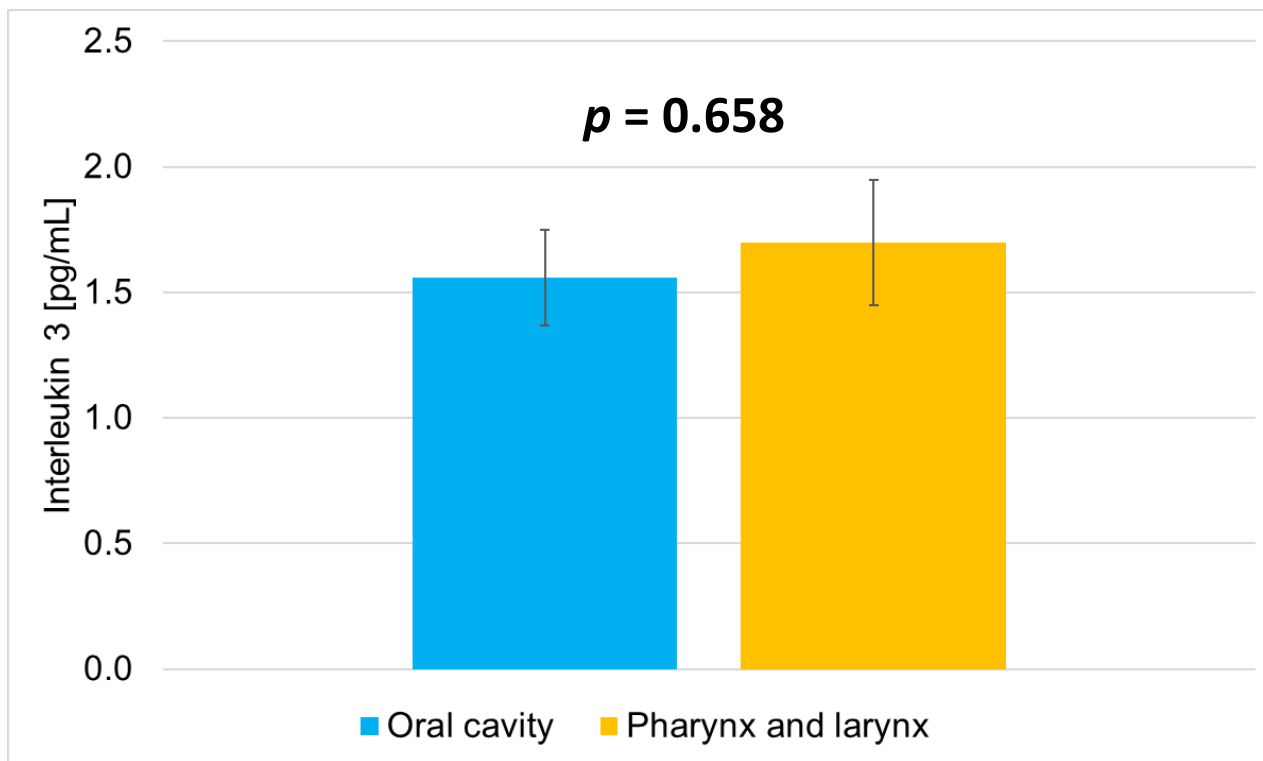


Introduction – characteristics of the study participants

Anthropometric characteristic of the patients with head and neck cancer divided according to the localization of the tumor. Each value is mean \pm SEM.

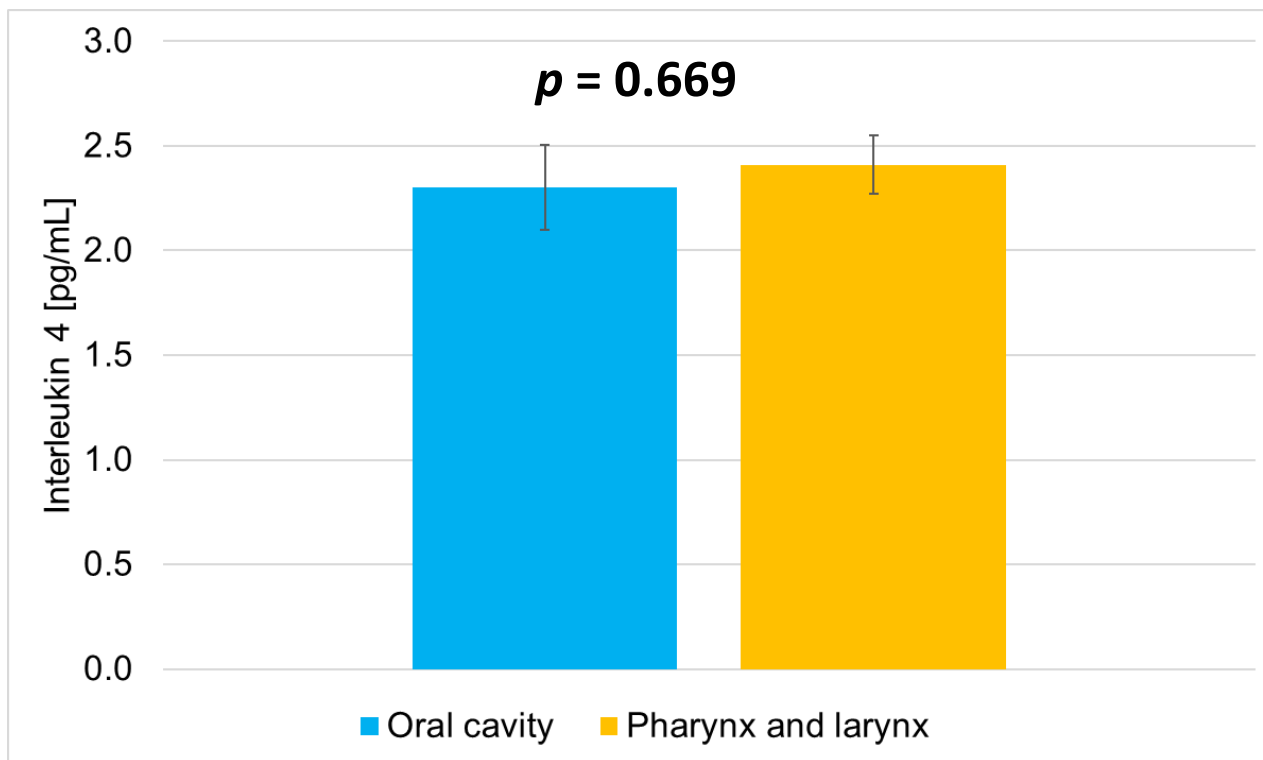
	Oral cavity (OC)	Pharynx and larynx (PL)	<i>p</i>
<i>n</i> (localization)	20 (9 tongue, 6 salivary gland, 3 lip, 2 gum)	20 (13 pharynx, 7 larynx)	-
Sex (f / m)	5 / 15	5 / 15	1.000
Age [yrs]	67.20 \pm 1.64	61.65 \pm 2.23	0.052
Body mass [kg]	69.75 \pm 3.12	77.11 \pm 4.76	0.204
Height [cm]	170.20 \pm 1.73	168.47 \pm 1.95	0.495
BMI [kg/m ²]	23.94 \pm 0.85	26.89 \pm 1.29	0.067

Results and discussion – interleukin 3



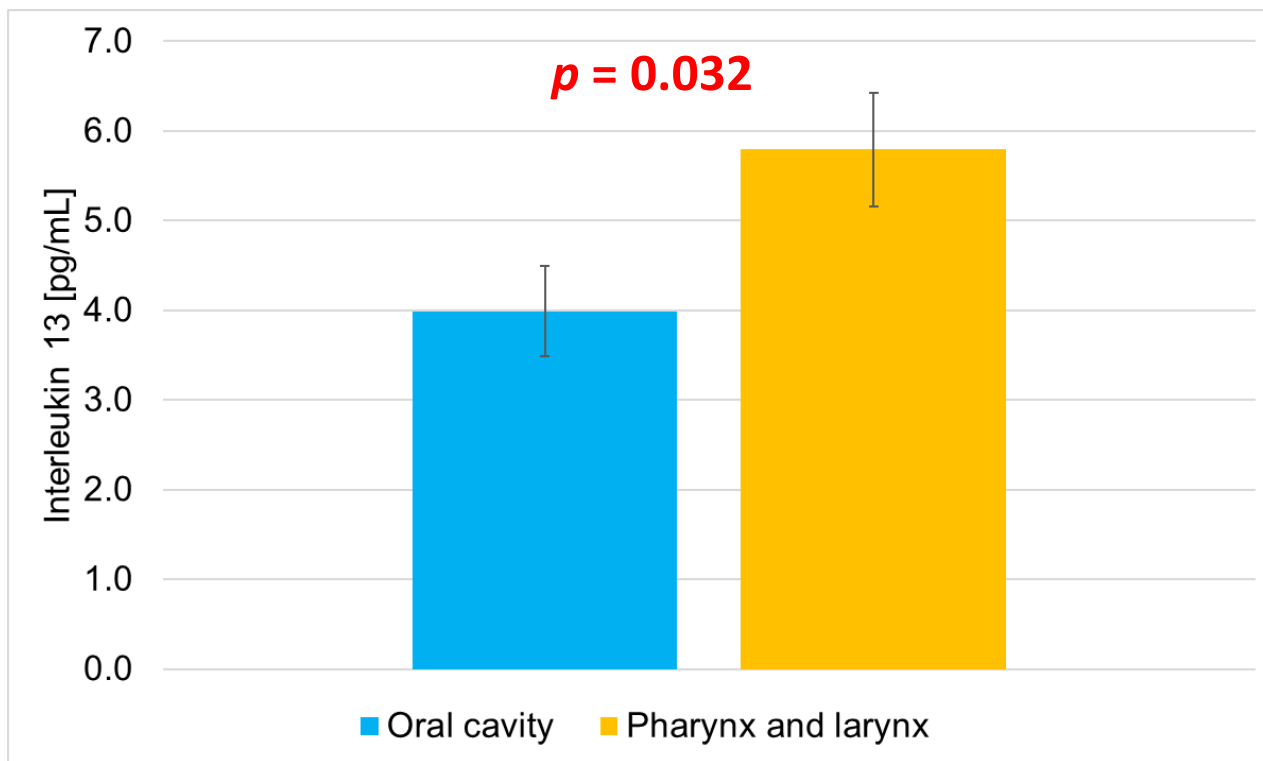
Interleukin 3 [pg/mL]	Oral cavity	Pharynx and larynx
Mean	1.559	1.698
SEM	0.190	0.249

Results and discussion – interleukin 4



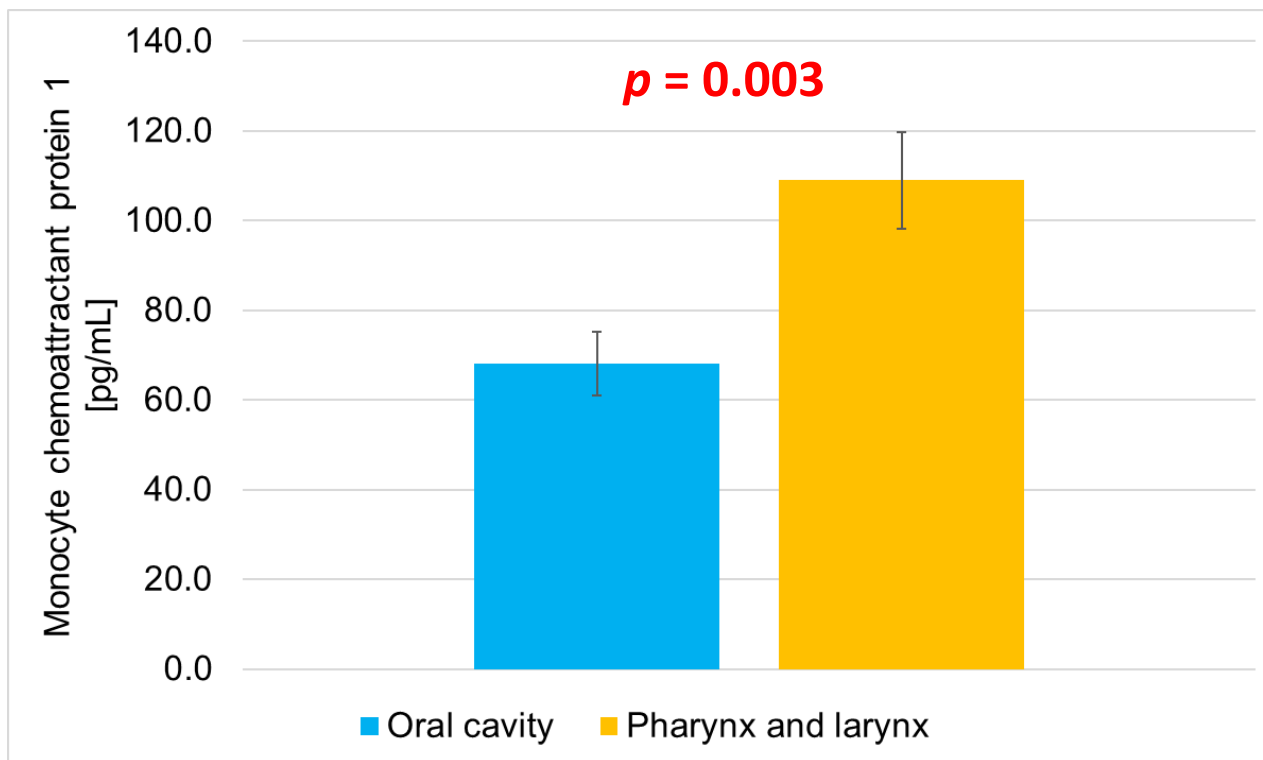
Interleukin 3 [pg/mL]	Oral cavity	Pharynx and larynx
Mean	2.301	2.410
SEM	0.202	0.140

Results and discussion – interleukin 13



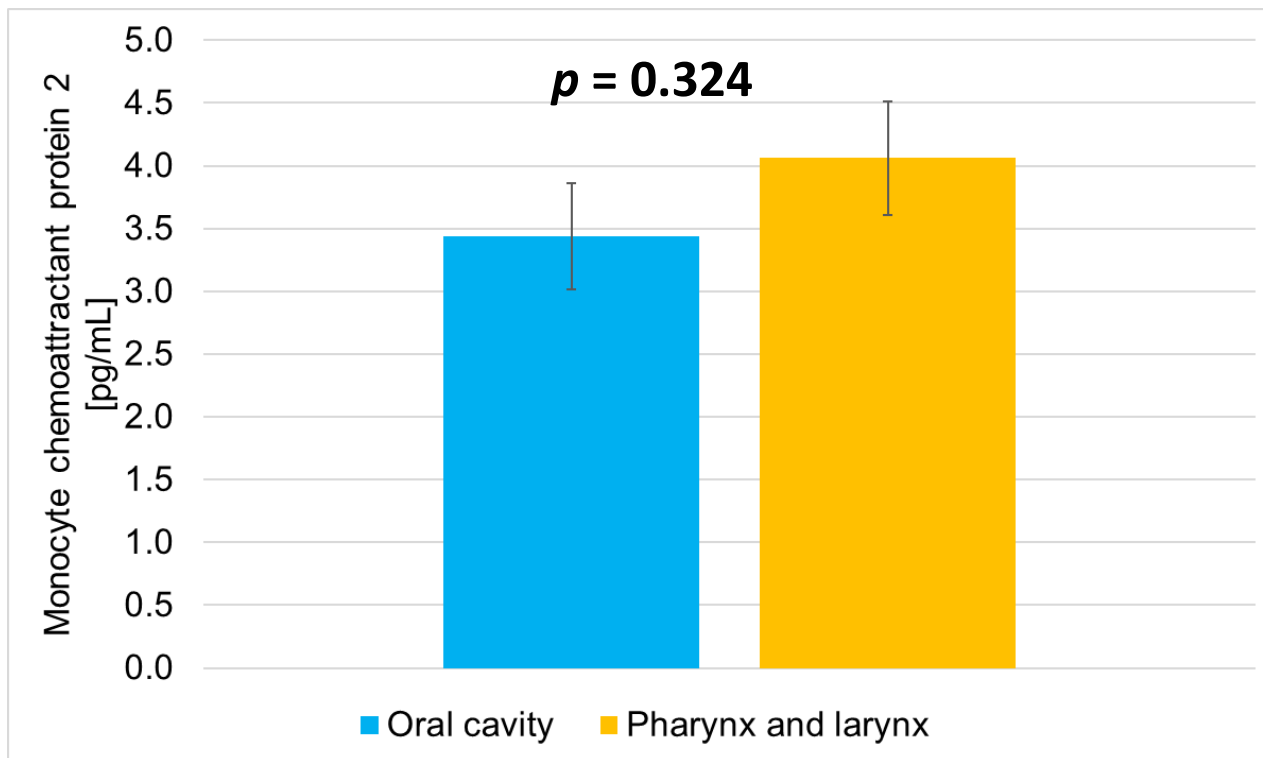
Interleukin 13 [pg/mL]	Oral cavity	Pharynx and larynx
Mean	3.991	5.791
SEM	0.501	0.636

Results and discussion – monocyte chemoattractant protein 1



Monocyte chemoattractant protein 1 [pg/mL]	Oral cavity	Pharynx and larynx
Mean	68.152	109.011
SEM	7.060	10.760

Results and discussion – monocyte chemoattractant protein 2



Monocyte chemoattractant protein 2 [pg/mL]	Oral cavity	Pharynx and larynx
Mean	3.440	4.061
SEM	0.425	0.453

Conclusions and discussion

- This study was limited to a small number of participants due to the low frequency of HNC.
- IL-13 and MCP-1 may be potential biomarkers to differentiate HNC due to the tumor localization.
- IL-13 presents broad biological activities partially similar to that of IL-4. IL-13 is mainly associated with airway diseases and has anti-inflammatory properties. In this study, we observed higher levels of IL-13 in the patients with tumors located in the pharynx and larynx. IL-13 induces a class of protein-degrading enzymes, namely matrix metalloproteinases (MMPs), in the airways.
- MCP-1, also known as chemokine (C-C motif) ligand 2, augments a monocyte anti-tumor activity. Numerous studies indicate that MCP-1 has pro-inflammatory properties and is involved in cancer progression.

Acknowledgments

This research was funded by the Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University, Poland, grant number ZES.WL.10.2021.



**NICOLAUS COPERNICUS
UNIVERSITY
IN TORUŃ**

Faculty of Medicine
Collegium Medicum in Bydgoszcz

**ECMC
2022**

**The 8th International Electronic
Conference on Medicinal Chemistry**

01-30 NOVEMBER 2022 | ONLINE

References

1. Chow, L.Q.M. Head and Neck Cancer. *N. Engl. J. Med.* **2020**, *382*, 60–72, doi:10.1056/NEJMra1715715.
2. Dougan, M.; Dranoff, G.; Dougan, S.K. GM-CSF, IL-3, and IL-5 Family of Cytokines: Regulators of Inflammation. *Immunity* **2019**, *50*, 796–811, doi:10.1016/j.immuni.2019.03.022.
3. Hallett, M.A.; Venmar, K.T.; Fingleton, B. Cytokine Stimulation of Epithelial Cancer Cells: The Similar and Divergent Functions of IL-4 and IL-13. *Cancer Res.* **2012**, *72*, 6338–6343, doi:10.1158/0008-5472.CAN-12-3544.
4. Hao, Q.; Vadgama, J. V.; Wang, P. CCL2/CCR2 signaling in cancer pathogenesis. *Cell Commun. Signal.* **2020**, *18*, 82, doi:10.1186/s12964-020-00589-8.
5. May, R.D.; Fung, M. Strategies targeting the IL-4/IL-13 axes in disease. *Cytokine* **2015**, *75*, 89–116, doi:10.1016/j.cyto.2015.05.018.
6. Mehanna, H.; Paleri, V.; West, C.M.L.; Nutting, C. Head and neck cancer-Part 1: Epidemiology, presentation, and preservation. *Clin. Otolaryngol.* **2011**, *36*, 65–68, doi:10.1111/j.1749-4486.2010.02231.x.
7. Shi, J.; Song, X.; Traub, B.; Luxenhofer, M.; Kornmann, M. Involvement of IL-4, IL-13 and Their Receptors in Pancreatic Cancer. *Int. J. Mol. Sci.* **2021**, *22*, 2998, doi:10.3390/ijms22062998.
8. Singh, S.; Anshita, D.; Ravichandiran, V. MCP-1: Function, regulation, and involvement in disease. *Int. Immunopharmacol.* **2021**, *101*, 107598, doi:10.1016/j.intimp.2021.107598.
9. Yoshimura, T. The chemokine MCP-1 (CCL2) in the host interaction with cancer: a foe or ally? *Cell. Mol. Immunol.* **2018**, *15*, 335–345, doi:10.1038/cmi.2017.135.