660MO Molecular targets in salivary gland cancers: A comprehensive genomic analysis of 1,666 cases

A. Sivapiragasam[1], P. Ashok Kumar[2], M. Bou Zerdan[3], D.J. Zaccarini[4], N.A. Danziger[5], J.S. Ross[5]

[1]Medical Oncology, SUNY Upstate Medical University, Syracuse, NY, USA; [2]Hematology-Oncology, SUNY Upstate Medical University, Syracuse, NY, USA; [3]Internal Medicine, SUNY Upstate Medical University, Syracuse, NY, USA; [4]Pathology, SUNY Upstate Medical University, Syracuse, NY, USA; [5]Pathology Department, Foundation Medicine, Inc, Cambridge, MA, USA

Background: Next Generation Sequencing (NGS) to identify key molecular targets is an important aspect of management in advanced Salivary Gland Carcinomas (SGC).

Methods: DNA was extracted from tissues of advanced SGC and Comprehensive Genomic Profiling (CGP) was done to evaluate for base substitutions, short insertions, deletions, copy number changes, gene fusions and rearrangements. Tumor Mutation Burden (TMB) was calculated on up to 1.25 Mb.

Results: The table shows the descriptive analysis of 1,666 SGC with clinically relevant Genomic Alterations (GA). Adenoid Cystic Carcinoma (ACC) (28.3%) was the commonest subtype. *CDKN2A* and *CDKN2B* GA were common in Acinic cell carcinoma (AcCC) (59 and 37.4%) and mucoepidermoid carcinoma (MEC) (52.5 and 30.5%). PIK3CA was common in Ductal Ca (32.6%) and High-grade Ca NOS (21.3%), making agents like Alpelisib, a consideration. *ERBB2* amplification/Short Variants (amp/SV) were frequent in Carcinoma ex Pleomorphic Adenoma (Ca ex PA) (17.6/9.8%) and Ductal Ca (16.3/3.6%). *ERBB2* directed therapies can play a crucial role in their management. *BRAF* GA was common in Ductal Ca (5.6%) and ACC (3.6%). Targets including *RET*, *FGFR*, *NTRK*, *BRCA* and *EGFR* had a low incidence. TMB >10 was common in High-grade NOS (18.3%) and MEC (16.9%). High PDL1 was also common in High grade NOS (8.9%) making us believe that this subtype may have the best response to immunotherapy (IO).

Conclusions: This large dataset reveals many opportunities for IO and targeted therapy contributing to the continuing increased precision in the selection of treatment for these patients.

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661MO Evaluation of the DNA damage response (DDR) network as predictor of nivolumab efficacy in head and neck squamous cell carcinoma (HNSCC)

P. Economopoulou[1], C. Papanikolaou[2], A. Spathis[3], I. Kotsantis[4], N. Gavrielatou[5], M. Anastasiou[6], D. Stellas[2], I. Panayiotides[3], P. Foukas[7], V.L. Souliotis[2], A. Psyrri[1]

[1]Oncology Unit, 2nd Department of Internal Medicine, Attikon University Hospital, Haidari, Greece; [2]Institute of Chemical Biology, National Hellenic Research Foundation, Athens, Greece; [3]Second Department of Pathology, Attikon University Hospital, Haidari, Greece; [4]2nd Propaedeutic Internal Medicine Clinic & Research Unit - Oncology Unit, Attikon University Hospital, Haidari, Greece; [5]Oncology Unit, 2nd Propaedeutic Clinic of Internal Medicine, Attikon University Hospital, Athens, Greece; [6]2nd Propedeutic Pathology Department, Attikon University Hospital, Athens, Greece; [7]Oncology, CHUV - Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland

Background: We have previously shown that Peripheral Blood Mononuclear Cells (PBMCs) from HNSCC patients, at diagnosis, exhibit deregulated DDR-related parameters and higher levels of oxidative stress compared to healthy individuals. Herein, we tested the hypothesis that aberrations in DDR signals of the patients' PBMCs may predict therapeutic benefit from PD-1 checkpoint blockade in HNSCC.

Methods: Oxidative stress, DDR associated parameters, including endogenous DNA damage and basal DNA repair mechanisms, namely nucleotide excision repair (NER) and double-strand breaks (DSBs) repair, were evaluated in PBMCs from 50 recurrent/metastatic HNSCC patients who participated in a phase II nivolumab trial (NCT03652142) and 26 healthy controls (HC). PBMCs were obtained at baseline, after 4 weeks of nivolumab treatment, and at progression.

Results: Per our previous findings, we verified that PBMCs from patients at baseline showed significantly higher levels of endogenous DNA damage compared with HC. Using alkaline comet assay measuring single-strand breaks and/or double-strand breaks, we found that lower endogenous DNA damage was associated with longer PFS (P=0.006), OS (P=0.002), and higher likelihood for response (P=0.03) and clinical benefit from nivolumab (P=0.015). Using γH2AX immunofluorescence staining for the evaluation of DSBs, we found that lower DSBs burden at baseline was also associated with statistically significant improvement of PFS, OS, and higher likelihood for response and clinical benefit (all $p < 0.002$). Moreover, PBMCs which exhibited lower levels of oxidative stress were correlated with a better clinical benefit (P=0.011). More importantly, lower NER and DSBs repair capacities of patients' PBMCs were associated with better PFS and OS and a higher likelihood for response and clinical benefit (all P<0.004).

Conclusions: Oxidative stress and DDR-related aberrations, measured in PBMCs from HNSCC patients correlated with the response to PD-1 immune checkpoint blockade. These results provide a proof of concept that DDR-based measurements could be used as a potential non-invasive biomarker to select HNSCC patients for treatment with PD-1 checkpoint inhibitors.

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662P Deep learning-enabled precise recurrence detection in nasopharyngeal carcinoma: A multicentre study

Y. Huang[1], Y. Deng[2], C. Li[2], X. Guo[1], X. Lv[1]

[1]Nasopharyngeal Carcinoma, Sun Yat-sen University Cancer Center, Guangzhou, China; [2]Artificial Intelligence Laboratory, Sun Yat-sen University Cancer Center, Guangzhou, China

Background: Precise recurrence detection facilitates timely intervention and prolongs survival in survivors with cured nasopharyngeal carcinoma (NPC). We presented an aide simultaneously reconciles dynamic risk probabilities profile and precise recurrence detection utilizing longitudinal magnetic resonance (MR) scans in NPC.

Table: 660MO

	N=1,666	GA (%)										
		CDKN2A	*CDKN2B*	*BRAF*	*PTEN*	*PIK3CA*	*ERBB2* (amp/SV)	*FGFR1*	*FGFR2*	*AR*	TMB > 10	PD-L1 High
ACC	471	3.8	2.4	1	3.1	8.6	0.2/0	1.2	4.1	0	0.2	0
AcCC	195	59	37.4	3.6	9.7	2.1	0.5/0	0	0.5	0.5	1.5	3
MEC	118	52.5	30.5	1.7	7.6	16.9	5.9/0	5.1	0	0	16.9	4.2
Myoepi-thelial Carcinoma	55	32.7	23.6	1.8	1.8	9.1	0/0	5.5	7.3	0	7.3	6.3
Ductal Ca	337	24	15.4	5.6	18.1	32.6	16.3/3.6	2.1	1.8	1.2	9.4	3
AdenoCa NOS	152	26.3	19.1	2	7.9	20.4	10.5/2.6	0.7	2	0	5.9	4.4
High Grade Ca NOS	240	22.9	14.6	2.9	10.8	21.3	15.8/2.1	4.2	2.1	0.4	18.3	8.9
Ca ex PA	51	13.7	9.8	2	19.6	11.8	17.6/9.8	11.8	7.8	0	11.8	0
Basaloid Ca	47	10.6	8.5	0	2.1	10.6	0/0	2.1	8.5	0	8.5	0