O001

Neoadjuvant and adjuvant pembrolizumab plus standard of care (SOC) in resectable locally advanced head and neck squamous cell carcinoma (LA HNSCC): phase 3 KEYNOTE-689 study

Dr. Ravindra Uppaluri[1,2], Dr. Robert I. Haddad[1,2], Dr. Yungan Tao[3], Dr. Christophe Le Tourneau[4], Dr. Nancy Y. Lee[5], Dr. William Westra[6], Dr. Rebecca Chernock[7], Dr. Makoto Tahara[8], Professor Kevin Harrington[9], Dr. Arkadiy L. Klochikhin[10], Dr. Irene Braña[11], Dr. Gustavo Vasconcelos Alves[12], Dr. Brett G. M Hughes[13], Dr. Marc Oliva[14], Dr. Iane Pinto Figueiredo Lima[15], Dr. Tsutomu Ueda[16], Dr. Tomasz Rutkowski[17], Dr. Ursula Schroeder[18], Dr. Paul-Stefan Mauz[19], Dr. Thorsten Fuereder[20], Dr. Simon Laban[21], Dr. Nobuhiko Oridate[22], Dr. Aron Popovtzer[23], Dr. Nicolas Mach[24], Dr. Yevhen Korobko[25], Dr. Diogo Alpuim Costa[26], Dr. Anupama Hooda-Nehra[27], Dr. Cristina P. Rodriguez[28], Dr. R. Bryan Bell[29], PhD Cole Manschot[30], Dr. Kimberly Benjamin[30], Dr Burak Gumuscu[30], Dr. Douglas Adkins[7]
[1]Brigham and Women's Hospital and Harvard Medical School, [2]Dana-Farber Cancer Institute, [3]Institut Gustave Roussy, [4]Institut Curie, [5]Memorial Sloan Kettering Cancer Center, [6]Icahn School of Medicine at Mount Sinai Hospital, [7]Washington University School of Medicine, [8]National Cancer Center Hospital East, [9]Institute of Cancer Research, [10]Yaroslavl Regional Clinical Oncology, [11]Vall d'Hebron Institute of Oncology (VHIO)/Vall d'Hebron University Hospital, [12]Centro Integrado de Pesquisa em Oncologia, Hospital Nossa Senhora de Conceição, [13]Royal Brisbane and Women's Hospital and University of Queensland, [14]Institut Català d'Oncologia (ICO) L´Hospitalet and Institut d'Investigació Biomèdica de Bellvitge (IDIBELL), [15]CRIO–Centro Regional Integrado de Oncologia, [16]Hiroshima University Hospital, [17]Maria Sklodowska-Curie National Research Institute of Oncology Gliwice branch, [18]Department of Oto-Rhino-Laryngology & Head and Neck Surgery, University of Luebeck, [19]Department of Otolaryngology, Head and Neck Surgery, University Hospital Tübingen, [20]Medical University of Vienna, [21]Department of Otorhinolaryngology and Head & Neck Surgery, Ulm University Medical Center and Comprehensive Cancer Center Ulm, [22]Yokohama City University School of Medicine, [23]Hadassah Medical Center, Ein Kerem, [24]Geneva University Hospital and University of Geneva, [25]SNPE National Cancer Institute, [26]Hospital CUF Descobertas, [27]Rutgers Cancer Institute of New Jersey, [28]University of Washington/Fred Hutchinson Cancer Center, [29]Providence Cancer Institute, Earle A. Chiles Research Institute, [30]Merck & Co., Inc.

Objectives: Neoadjuvant and adjuvant immune checkpoint inhibitors added to SOC (surgery + postoperative radiotherapy [PORT] ± concurrent chemotherapy) yielded promising efficacy results in participants with LA HNSCC in early phase studies. The randomized, open-label, phase 3 KEYNOTE-689 study (NCT03765918) evaluates neoadjuvant and adjuvant pembrolizumab + SOC vs SOC in this population.

Methods: Adults with newly diagnosed resectable LA HNSCC (larynx/hypopharynx/oral cavity stage III/IVA; oropharyngeal stage III/IVA p16− or stage III T4 N0-2 p16+) were randomized 1:1 to 2 cycles neoadjuvant and 3 cycles concurrent (during PORT) and 12 cycles adjuvant pembrolizumab 200 mg IV Q3W + SOC vs SOC. SOC included surgery for all participants + PORT 60 Gy in 30 fractions for low-risk, PORT 66 Gy in 33 fractions + 3 cycles concurrent cisplatin 100 mg/m2 Q3W for high-risk, and PORT 70 Gy in 35 fractions + cisplatin for gross residual disease. The primary endpoint is event-free survival (EFS) per RECIST 1.1 by blinded independent central review. Key secondary endpoints are major pathological response (mPR; ≤10% invasive SCC) by blinded independent pathologist review and overall survival (OS). Efficacy endpoints are sequentially assessed in 3 populations: participants with tumors with PD-L1 combined positive score (CPS) ≥10, CPS ≥1, and all participants. Treatment-related adverse events are graded per CTCAE v4.03.

Results: From December 2018 to October 2023, 363 participants were randomized to pembrolizumab + SOC and 351 to SOC. As of 25 July 2024 (first interim analysis), median follow-up was 38.3 months (range, 9.0–66.5). Baseline demographics were balanced between arms. The CPS ≥10 population included 234 participants in the pembrolizumab + SOC arm and 231 in the SOC arm; the CPS ≥1 population included 347 and 335 participants, respectively. EFS (CPS ≥10: median 59.7 vs 26.9

months, HR 0.66, 95% CI 0.49–0.88, P=.00217; CPS ≥1: 59.7 vs 29.6 months, HR 0.70, 95% CI 0.55–0.89, P=.00140; all participants: 51.8 vs 30.4 months, HR 0.73, 95% CI 0.58–0.92, P=.00411) and mPR rate difference (CPS ≥10: 13.7%, 95% CI 9.7–18.7, P<.00001; CPS ≥1: 9.8%, 95% CI 7.0–13.3, P<.00001; all participants: 9.3%, 95% CI 6.7–12.8, P<.00001) analyses were statistically significant with pembrolizumab + SOC vs SOC in all prespecified populations. Additional follow-up for OS is ongoing. Grade ≥3 treatment-related adverse event frequency was similar (44.6% with pembrolizumab + SOC vs 42.9% with SOC); 4 and 1 deaths occurred due to treatment-related adverse events, respectively. Immune-mediated AEs occurred in 43.2% of participants with pembrolizumab + SOC, most commonly hypothyroidism (24.7%).

Conclusions: Adding neoadjuvant and adjuvant pembrolizumab to SOC significantly improved EFS and mPR rate difference in participants with resectable LA HNSCC independent of CPS. The safety profile of pembrolizumab was consistent with expectations.

O002

Safety and efficacy of first-line dostarlimab monotherapy in patients with programmed death ligand 1 (PD-L1)-positive recurrent/metastatic head and neck squamous cell carcinoma (HNSCC): GALAXIES H&N-202 interim analysis

Dr Paolo Bossi[1,2], Dr Lillian L Siu[3], Dr Makoto Tahara[4], Dr Nicholas Ramscar[5], Dr Hamza Khan[6], Dr Micki Hill[7], Dr Steven Pattishall[8], Dr Gary Carlson[9], Dr Arindam Dhar[10], Dr Robert Haddad[11]
[1]Humanitas University, [2]IRCCS Humanitas Research Hospital, [3]Princess Margaret Cancer Center, University Health Network, University of Toronto, [4]National Cancer Center Hospital East, [5]GSK, [6]GSK, [7]GSK, [8]GSK, [9]GSK, [10]GSK, [11]Dana Farber Cancer Institute, Harvard Medical School

Objectives: Immune checkpoint inhibitors have improved outcomes for patients with recurrent or metastatic HNSCC [1–3]; however, overall survival for recurrent/metastatic disease remains poor. GALAXIES H&N-202 (NCT06062420) is a Phase 2 platform study evaluating the safety and efficacy of novel immunotherapy combinations versus dostarlimab monotherapy as first-line treatment in patients with recurrent/metastatic PD-L1-positive HNSCC. Here, we report the first interim results for patients who were randomised to the dostarlimab monotherapy arm.

Methods: GALAXIES H&N-202 is an open-label, Phase 2 platform study evaluating novel immunotherapy combinations in patients with PD-L1-positive (combined positive score [CPS] ≥1) recurrent/metastatic HNSCC previously untreated in this setting. Patients randomised to the dostarlimab monotherapy arm received dostarlimab 500 mg every 3 weeks until progression, unacceptable toxicity, death or withdrawal. The primary endpoint was investigator-confirmed objective response rate (ORR) per Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1. Safety was a secondary endpoint.

Results: At data cutoff (20 March 2025), 161 patients had been enrolled into the trial and had at least 4.5 months of follow-up data from first dose. Among this cohort, 41 patients were randomised to the dostarlimab monotherapy arm (mean age 65.7 years; 71% male). After a median (range) of 18.0 (3–54) weeks of treatment, ORR in this cohort of patients was 26.8% (95% confidence interval [CI]: 14.2, 42.9) (Table 1). Treatment-emergent adverse events (TEAEs) were reported in 90% (n=37) of patients, with 54% (n=22) of patients reported to have treatment-related adverse events (TRAEs; Table 2). Grade 3+ TEAEs occurred in 34% (n=14) of patients, with 5% (n=2) of patients reported to have Grade 3+ TRAEs. Overall, 5% (n=2) of patients experienced treatment-related serious adverse events (SAEs), and 5% (n=2) of patients discontinued treatment due to TEAEs. There were 5 fatal SAEs, none of which were treatment related.

Conclusion: In this interim analysis, dostarlimab monotherapy showed anti-tumour activity in HNSCC with a safety profile similar to that observed for other immune checkpoint inhibitors used in HNSCC [1–3]. Results for additional substudy arms and from additional patients in the dostarlimab monotherapy arm will be reported in future.

References:

1. Ferris RL, et al. N Engl J Med 2016;375(19):1856–67.
2. Cohen EEW, et al. Lancet 2019;393(10167):156–67.
3. Burtness B, et al. Lancet 2019;394(10212):1915–28.

Funding: This study (NCT06062420; GSK Study 219885) was funded by GSK. Medical writing support was provided by Avalere Health, funded by GSK.

Table 1: Efficacy outcomes

	Dostarlimab monotherapy (n=41)
Confirmed ORR, n (%), 95% CI	11 (26.8) 14.2, 42.9
Best response, n (%)	
Complete response	1 (2.4)
Partial response	10 (24.4)
Stable disease	17 (41.5)
Progressive disease	7 (17.1)
Not evaluable	6 (14.6)
Confirmed ORR by CPS score, n (%)	
CPS 1–19 (N=21)	3 (14)
CPS ≥20 (N=20)	8 (40)

CI, confidence interval; CPS, combined positive score; ORR, objective response rate.

Table 2: Safety outcomes

n (%)	Dostarlimab monotherapy (n=41)
Any TEAE	37 (90)
Any TRAE	22 (54)
Any Grade 3+ TEAE	14 (34)
Any Grade 3+ TRAE	2 (5)
TEAEs leading to treatment discontinuation	2 (5)
TEAEs leading to dose interruption/delay	9 (22)
Any treatment-emergent SAEs	13 (32)
Any treatment-related SAEs	2 (5)
Fatal SAEs	5 (12)
Treatment-related fatal SAEs	0

SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

O003

Single Vocal Cord Irradiation (SVCI) vs Whole Laryngeal radiotherapy in the treatment of T1aN0 glottic cancer A prospective randomized trial

Dr Mohamed Elsharief[1], Prof Ashraf Hassouna[1], Dr Sherweif Mohamed[1], Mr Abdelrahman Mosallam[2], Prof Amr Elbadrawy[3], Dr Ashraf Shawky[4], Prof Tarek Shouman[1]
[1]Radiation oncology department, National Cancer Institute Cairo University, [2]Medical Physics Unit, Radiation Oncology department, Cairo University, [3]Otorhinolaryngology department Faculty of Medicine Cairo University, [4]Surgical Oncology department, National Cancer Institute, Cairo University

Background

Both TLS and radiotherapy are used in the treatment of T1aN0 glottic cancer with similar oncological outcomes. In contrast to millimetric margins used in TLS, the standard radiotherapy field still relies on classic 2D box field exposing the whole larynx to full radiation dose. Retrospective studies suggest excellent local control with single vocal cord irradiation that targets only the affected vocal cord. So the aim of this study was to compare the treatment outcome and toxicity of the classic radiotherapy field vs single vocal irradiation technique

Patients and methods

This is a prospective phase 2 randomized study (clinicaltrial.gov registration NCT05679856)

58 consecutive patients with T1N0 glottic cancer were included. 29 were randomised to standard of care whole larynx radiotherapy field that covers the whole larynx with a prescription dose of 63Gy/28Fs while the other 29 patients were randomised to single vocal irradiation field with a prescription dose of 58.08Gy/16Fs. Baseline voice handicap index was recorded before treatment, at end of radiotherapy then during each follow up visit.

2

Results

Demographic and patients characteristics were comparable between the 2 arms.

The dose to different organs at risk such as the contralateral vocal cord, arytenoid and supraglottic larynx were statistically lower in the SVCI arm. 2 year local control rate was 100% in SVCI arm and 96% in the whole larynx arm, with no statistical significant difference. No grade 3 or 4 toxicities were reported in both treatment arms. VHI scores were comparable at baseline and at end of radiotherapy, but it was statistically significant better at 2 months post treatment and thereafter in the SVCI arm as compared to the whole larynx arm

Conclusion

SVCI is effective and safe treatment for T1aN0 glottic cancer with excellent local control rates and safe toxicity profile. Reported voice quality is much better with SVCI probably due to sparing of laryngeal substructures. Multicenter studies with larger sample size are needed to confirm study results so that SVCI could be standard of care in T!aN0 glottic cancer radiotherapy.

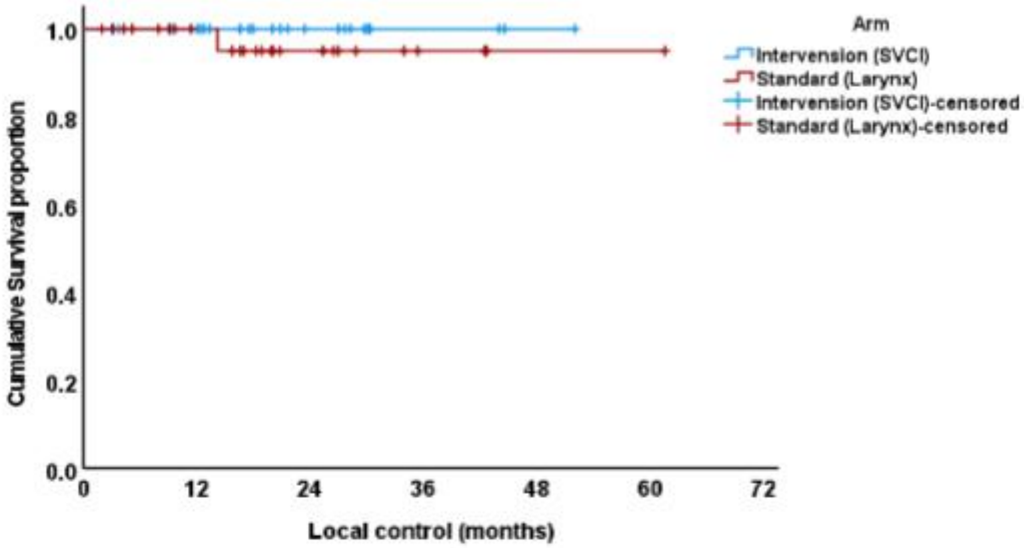

Figure 1: Local control in relation to treatment arm

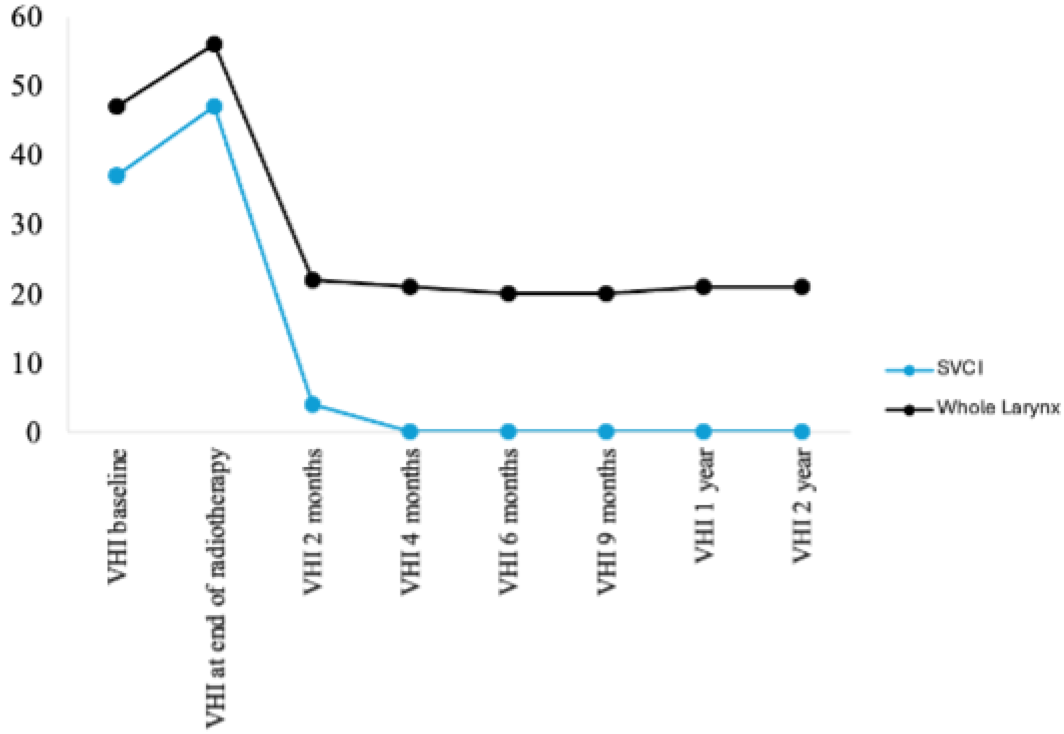

Figure 2: Box plot representing VHI score among study groups.

O004

Retifanlimab (Anti–PD-1 mAb) Alone Or In Combination With Anti-LAG3 ± Anti-TIM3 mAbs In Previously Untreated, Recurrent And/Or Metastatic (R/M) PD-L1+ HNSCC: A Double-Blind Randomised Controlled Phase 2 Trial

Prof. Denis Soulières[1], Prof. Robert Haddad[2], Dr. Amiran Matitashvili[3], Dr. Ching Y Hsieh[4], Prof. Amanda Psyrri[5], Dr. Hui-Ching Wang[6], Dr. Huai-Cheng Huang[7], Dr. Francesco Perri[8], Prof. Prakash Neupane[9], Dr. Javier Caballero[10], Dr. Amaury Daste[11], Dr. Elena Fountzilas[12], Dr. Claudia Vierira[13], Dr. Varinder Kaur[14], Mr. Richard Schaub[15], Dr. Lulu Cheng[15], Dr. Nawel Bourayou[16], Dr. Louis Viviers[16], Prof. Christophe Le Tourneau[17]
[1]Haematology/Oncology, Centre Hospitalier de l'Université de Montréal, [2]Dana-Farber Cancer Institute, Brigham and Women's Hospital, Harvard Medical School, [3]Mardaleishvili Medical Center, [4]Division of Hematology and Oncology, Department of Medicine, China Medical University Hospital, [5]2nd Department of Internal Medicine, Attikon Hospital, National Kapodistrian University of Athens, [6]Division of Hematology and Oncology, Department of Internal Medicine, Kaohsiung Medical University Hospital, [7]National Taiwan University Hospital and College of Medicine, [8]Head and Neck Medical Oncology Unit, Istituto Nazionale Tumori, IRCCS Fondazione G. Pascale, [9]The University of Kansas Medical Center, [10]Medical Oncology, Hospital Universitari i Politècnic La Fe, [11]Department of Medical Oncology, Hôpital Saint-André, CHU Bordeaux-University of Bordeaux, [12]Department of Medical Oncology, St Lukes's Clinic, [13]Instituto Português de Oncologia do Porto Francisco Gentil (IPO-PORTO), [14]University of Virginia Cancer Center, [15]Incyte Corporation, [16]Incyte Biosciences International Sàrl, [17]Department of Drug Development and Innovation (D3i), Institut Curie; INSERM U900 Research Unit; Faculty of Medicine, Paris-Saclay University
Objectives: PD-1 inhibitors improve survival in patients (pts) with previously untreated R/M PD-L1+ HNSCC. The study assessed whether dual and triple immune checkpoint blockade improves efficacy in pts vs anti–PD-1 treatment (tx) alone.

Methods: Pts were randomised (1:1:1) to retifanlimab (RETI) alone, or RETI with tuparstobart (anti-LAG3 mAb; doublet tx) or RETI + tuparstobart and verzistobart (anti-TIM3 mAb; triplet tx). Tx continued for up to 2 years or until investigator-determined progression by RECIST 1.1, unacceptable toxicity or withdrawal of consent. Primary endpoint: progression-free survival (PFS). Two primary hypotheses were tested: superiority of doublet and/or triplet tx, each vs RETI; 140 PFS events were needed for 80% power to test these hypotheses at 1-sided α of 0.05. Secondary endpoints included objective response rate (ORR), duration of response (DOR), overall survival (OS) and safety.

Results: 176 pts were randomised (RETI n=59, doublet tx n=60, triplet tx, n=57): central PD-L1 CPS ≥20, 57%; central LAG3 expression ≥5%, 55%; HPV+, 14%. At data cutoff (28 Jan 2025; estimated median follow-up time, 14 months [mo]), median PFS was 5.8 mo (95% CI, 3.7, 7.6) with doublet tx vs 5.6 mo (95% CI, 3.5, 9.7) with RETI alone (HR, 1.05; 95% CI, 0.66, 1.67; P=0.59), and 5.3 mo (95% CI, 2.1, 7.9) with triplet tx (HR vs RETI alone, 1.09; 95% CI, 0.69, 1.72; P=0.64). Confirmed ORR was numerically higher with triplet (32% [95% CI, 19.9, 45.2]) and doublet tx (30% [95% CI, 18.8, 43.2]) vs RETI (20% [95% CI, 11.0, 32.8]). Difference in ORR was 11.2% (95% CI, –4.8, 26.6) for triplet vs RETI and 9.7% (95% CI, –6.1, 24.7) for doublet vs RETI. DOR and OS data are not mature. In the RETI, doublet and triplet tx groups, respectively, grade 3/4 tx-related AEs occurred in 16%, 12% and 21% of pts; any-grade immune-related AEs occurred in 38%, 43% and 47% of pts.

Conclusions: This randomised phase 2 trial showed that adding anti-LAG3 ± anti-TIM3 did not significantly improve PFS vs RETI alone in pts with previously untreated R/M PD-L1+ HNSCC. Median PFS with RETI alone exceeded historical data from studies of other anti–PD-1 tx in R/M HNSCC.

O005

Comparison of Conventional Radiotherapy and VMAT with Different PTV Margins for Early Glottic Cancer: Dosimetric and Clinical Outcomes

MD Xuanhe Hou[1], MSc Ellen Bos[1], PhD Leonard Wee[1], MD Frederik Wesseling[1], MD, PhD Jolien Heukelom[1], PhD Ans Swinnen[1], Rik Emmahl[1], Prof. Laura Baijens[2,3], Ruud Houben[1], MD,PHD Frank Hoebers[1]

[1]Department of Radiation Oncology (MAASTRO), GROW - Research Institute for Oncology and Reproduction, Maastricht University, Maastricht, the Netherlands, [2]Department of Otorhinolaryngology, Head and Neck Surgery, Maastricht University Medical Center, Maastricht, the Netherlands, [3]GROW- Research Institute for Oncology and Reproduction, Maastricht University, Maastricht, the Netherlands

Purpose/Objectives

Local radiotherapy (RT) for early glottic cancer was traditionally delivered with standard lateral beams encompassing the entire larynx. With the introduction of conformal techniques such as volumetric modulated arc therapy (VMAT), more targeted approaches have become routine. However, evidence directly comparing treatment-related toxicity between conventional RT and VMAT remains limited, and few studies have assessed whether reducing planning target volume (PTV) margins in VMAT can mitigate toxicity while preserving local control. In this retrospective cohort study, we compared conventional RT, VMAT with wider PTV margins, and VMAT with narrower PTV margins to evaluate post-treatment outcomes.

Materials/Methods

Between 2010 and October 2024, 259 patients with early glottic cancer received local RT to a dose of 60-68 Gy in 2.0-2.4 Gy per fraction. We split the cohort in three groups depending on the RT techniques used during this period. Group 1 (n = 39) underwent conventional RT with two opposed lateral wedge-pair fields to the entire larynx. Group 2 (n = 106) received VMAT to a PTV with wide margins (10 mm in axial plane; 12 mm in craniocaudal direction) around the glottic (single cord) gross tumor volume (GTV)-based clinical target volume (CTV), using kV-kV verification with bony match on the vertebral column. Group 3 (n = 114) received VMAT to a PTV with smaller margins (respectively 3 mm axial and 5 mm craniocaudal) around the same CTV as in group 2, incorporating a “Do Not Swallow” instruction during VMAT and daily online cone-beam computed tomography (CBCT) verification with thyroid cartilage matching.

Side-effects and oncological outcomes were prospectively registered within the routine follow-up program (ClinicalTrials.gov Identifier: NCT01985984). Acute and late physician-rated toxicities were assessed using Common Terminology Criteria for Adverse Events (CTCAE) version 4, covering dysphagia, aspiration, xerostomia, weight loss, laryngeal oedema, mucositis, radiation dermatitis, neck fibrosis, osteonecrosis, and hypothyroidism.

Results

The median follow-up for patients alive at last follow-up was 120 months for group 1, 105 months for group 2, and 47 months for group 3. Doses to all relevant organs at risk (Dmeans) were significantly lower for group 3 compared with group 2, including the carotid arteries, spinal cord and the swallowing muscles, see table 1. Group 3 experienced significantly lower rates of most acute and late toxicities, including dysphagia, aspiration and mucositis, while no differences were observed in e.g. hypothyroidism or osteonecrosis (Table 2). There were no significant differences in local control ($p = 0.468$) and overall survival ($p = 0.141$) between the three groups. The 2- and 3-year local control rates were 94.4% and 90.9% for Group 1, 94.9% and 92.6% for Group 2, and 96.3% and 96.3% for Group 3. The corresponding 2- and 3-year overall survival rates were 94.7% and 92.1%, 93.3% and 87.5%, and 92.9% and 86.3%, respectively.

Conclusions

Compared to historical controls receiving RT with wider margins, early-stage glottic cancer patients receiving localized radiotherapy using VMAT with smaller PTV margins and daily CBCT-based matching resulted in lower toxicity rates, while maintaining high local control rates.

Keywords: radiotherapy, glottic cancer, intensity-modulated, toxicity

Table 1. DVH-derived OAR dose parameters (mean ± SD) for Group 2 (large-field VMAT) and Group 3 (small-field VMAT).

Organ at Risk	Dose metric	Group 2 Mean ± SD	Group 3 Mean ± SD	Mean Difference	95% CI of Difference	p-value
Carotid L	D0.03cc	44.5 ± 12.4	32.9 ± 15.1	11.1	7.4 – 14.8	<0.001
Carotid R	D0.03cc	44.9 ± 13.8	37.4 ± 14.0	8.2	4.4 – 11.9	<0.001
Spinal cord	D0.03cc	23.4 ± 7.1	15.2 ± 5.9	9	7.2 – 10.7	<0.001
Cervical esophagus	Dmean	6.8 ± 8.5	1.9 ± 2.4	4.9	3.2 – 6.5	<0.001
PCM inferior	Dmean	49.0 ± 10.1	25.3 ± 10.2	23.7	21.0 – 26.4	<0.001
PCM medial	Dmean	8.1 ± 11.2	2.7 ± 5.5	5.6	3.3 – 8.0	<0.001
PCM superior	Dmean	0.56 ± 0.44	0.23 ± 0.31	0.34	0.23 – 0.44	<0.001
Submandibular L	Dmean	1.72 ± 1.9	0.76 ± 1.6	1.01	0.56 – 1.46	<0.001
Submandibular R	Dmean	1.82 ± 2.2	1.00 ± 2.5	0.85	0.21 – 1.49	0.009
Supraglottic	Dmean	39.8 ± 9.2	24.7 ± 8.7	15.1	12.7 – 17.5	<0.001
Thyroid	Dmean	15.3 ± 9.2	8.5 ± 4.8	6.6	4.6 – 8.7	<0.001

Group comparisons were performed using independent-samples t-tests (Levene's test applied). DVH data were not available for Group 1 (conventional RT).

O006

Genome wide Copy Number Alterations in ctDNA as Novel Biomarker in Head and Neck Squamous Cell Cancer (IDENTIFY Trial)

Dr Francesca Gaino[1,2], Dr Erika Stucchi[1,2], Dr Cristina Gurizzan[2], Dr Federica Riva[2], Dr Riccardo Zadro[2], Dr Lara Paracchini[2], Dr Alessandro Salvi[3], Dr Luigi Lorini[2], Dr Carlo Resteghini[1,2], Dr Claudia Assoni[3], Dr Davide Smussi[3], Dr Andrea Alberti[3], Prof Davide Mattavelli[3], Prof Piero Nicolai[4], Dr Werner Garavello[5], Prof Livio Presutti[6], Dr Stefano Bondi[7], Dr Cristiana Bergamini[8], Prof Giorgio Peretti[9], Dr Sergio Marchini[2], Prof Giuseppe Spriano[1,2], Prof Giuseppe Mercante[1,2], Prof Paolo Bossi[1,2]
[1]Humanitas University, [2]Humanitas Research Hospital, [3]University of Brescia, [4]University of Padova, [5]University of Milano-Bicocca, [6]Azienda Ospedaliera Universitaria di Bologna IRCCS, [7]Candiolo Cancer Institute, FPO-IRCCS, [8]Fondazione IRCCS - Istituto Nazionale dei Tumori, [9]University of Genova

Background

New strategies to stratify the risk of Head and Neck Squamous Cell Cancer (HNSCC) beside clinical stage and HPV, as well to follow patients (pts) after treatments (Tx) are strongly awaited. Liquid biopsy is a promising, minimally invasive alternative to tissue biopsy for cancer diagnosis and monitoring. Aim of this study is to explore the potential of Genome wide Copy Number Alterations (CNA) in circulating tumor DNA (ctDNA), described as a tumor fraction (TF) of cell free DNA (cfDNA), in defining prognosis of HNSCC patients and for early identification of recurrence.

Methods

Pts with stage I-IV HNSCC before curative treatment were enrolled and underwent blood collections at baseline (T0) and during follow up (FU) at 3, 6, 12 and 18 months. cfDNA was isolated and purified from plasma, and shallow Whole Genome Sequencing was performed to identify regions of CNA. Subsequently, the % of ctDNA over total cfDNA (defined as TF) was obtained. Descriptive statistics and correlation analyses were performed in order to explore associations between ctDNA and clinical characteristics. We herein report the results of the baseline analysis of the first enrolled pts.

Results

Among enrolled pts between March 2021 and April 2025, 53 T0 blood samples were analysed. Two failures occurred, resulting in a failure rate of 3.8% with our technique. 51 pts (11 females) were included in the analyses. Median age was 63 years (39-85). HPV+ pts were 11 (21.6%). Stage distribution was as follows: I in 3 pts, II in 5 pts, III in 20 pts, IV in 23 pts. 32 pts underwent surgery + adjuvant Tx, and 19 pts (chemo)radiotherapy. Median FU was 26 months (1-43). 19 pts relapsed (37.3%) with a median time to relapse of 28 months. Median T0 TF was 5.3 (1.6-47.8) in the whole sample and 10.7 (3.9-37.8) in HPV+ pts. Analysis showed no correlation between TF at T0 and sex, age, smoking status, overall stage, and N stage. A non-significant trend toward higher T0 TF was observed in HPV+ pts ($p=0.08$). Pts who relapsed showed significantly higher TF values at T0 ($p=0.05$).

Discussion

Our technique proved to be feasible with a low failure rate. Baseline TF correlated with relapse in our pts. Further analyses are warranted to explore dynamic variations of TF during FU.

O007

Impact of Metastasis Directed Therapy with Locoregional Radiotherapy in De Novo Metastatic Nasopharyngeal Carcinoma

Dr Anuj Kumar[1], Dr Sarbani Ghosh Laskar[1], Dr Rahat Malhotra[1], Dr Shwetabh Sinha[1], Dr Samarpita Mohanty[1], Dr Ashwini Budrukkar[1], Dr Monali Swain[1], Dr Amiya Agrawal[1], Dr Rishi Mittal[1], Dr Kumar Prabhash[2], Dr Vanita Noronha[2], Dr Nandini Menon[2], Dr Minit Shah[2], Dr Amit Joshi[2]
[1]Department of Radiation Oncology, Tata Memorial Centre, Homi Bhabha National Institute,
[2]Department of Medical Oncology, Tata Memorial Centre, Homi Bhabha National Institute

Objectives:
De novo metastatic nasopharyngeal carcinoma (mNPC) has poor prognosis with systemic therapy alone. While locoregional radiotherapy (LRRT) improves survival, the role of metastasis-directed therapy (MDT) remains less defined.

Methods:
We retrospectively reviewed 54 patients with de novo mNPC treated from 2013-2024 at a tertiary cancer centre. All received platinum-based induction chemotherapy (NACT) followed by definitive LRRT. Seventeen patients (31%) also underwent MDT to metastases (SBRT, IMRT, or radiofrequency ablation). Patients were categorised as oligometastatic (≤5 lesions; n=30) or polymetastatic (>5; n=24). In the oligometastatic subgroup, outcomes with MDT (n=15) versus no MDT (n=15) were compared. Survival outcomes were estimated by Kaplan-Meier method, and multivariable Cox regression was performed.

Results:
At a median follow-up of 27 months, the estimated 2-year OS, RFS, and DRFS were 67.5%, 45.4%, and 52.7%, respectively. Oligometastatic disease was associated with superior 2-year RFS (59.2% vs 27.8%, p=0.007) and DRFS (69% vs 31.4%, p=0.004) compared with polymetastatic disease. In the overall cohort, MDT was associated with favourable OS, RFS, and DRFS. Within the oligometastatic subset (15 MDT vs 15 no MDT), outcomes appeared comparable, though interpretation is limited by sample size and event numbers. Patients achieving CR/PR after NACT had improved outcomes, whereas progression predicted poor survival. Maintenance capecitabine (44%) showed a trend towards OS benefit without RFS advantage. On multivariable analysis, MDT was independently associated with improved RFS (HR 0.27, p=0.047) and showed a trend towards improved OS (HR 0.25, p=0.072).

Conclusion:
Multimodality treatment integrating LRRT and MDT was feasible and associated with encouraging survival outcomes in de novo mNPC. Subgroup analysis of oligometastatic patients did not show a clear difference between MDT and non-MDT, reflecting limited statistical power. These findings support the inclusion of MDT into treatment strategies for de novo mNPC, while underscoring the need for validation in larger prospective trials.

O008

Genome-wide discovery and validation of novel DNA methylation markers for oral cancer detection using saliva

Dr. Óscar Rapado-González[1,2,3,4,5], Dr. Nicolás Costa-Fraga[6], Dr. Ángel Díaz-Lagares[3,4,6], Dr. José Luis López-Cedrún[7], Dr. Cláudia Araújo[8,13], Dr. Rosa Capelo[8,13], Dr. Margarida Lima[8,13], Dr. Cláudia Vieira[9,13], Ms. Aida Cardoso[10], Ms. Sandrina Nogueira[10], Dr. Jorge Guimarães[8,13], Ms. Catarina Martins Diz Lobo Ribeiro[11], Prof. Rui Henrique[5,12,13], Dr. Rafael López-López[3,4,14], Dr. Laura Muinelo-Romay[1,3,4], Prof. Carmen Jerónimo[5,13], Prof. María Mercedes Suárez-Cunqueiro[2,3,4,14], Dr. José Carlos Pereira[8]

[1]Liquid Biopsy Analysis Unit, Translational Medical Oncology Group (ONCOMET), Health Research Institute of Santiago de Compostela (IDIS), [2]Department of Surgery and Medical-Surgical Specialties, Medicine and Dentistry School, Universidade de Santiago de Compostela (USC), [3]Galician Precision Oncology Research Group (ONCOGAL), Medicine and Dentistry School, Universidade de Santiago de Compostela (USC), [4]Centro de Investigación Biomédica en Red en Cáncer (CIBERONC), Instituto de Salud Carlos III, [5]Cancer Biology & Epigenetics Group, Research Center of IPO Porto (CI-IPOP), Portuguese Oncology Institute of Porto (IPO Porto), Porto Comprehensive Cancer Center Raquel Seruca (Porto.CCC), [6]Epigenomics Unit, Cancer Epigenomics, Translational Medical Oncology Group (ONCOMET), Health Research Institute of Santiago de Compostela (IDIS), University Clinical Hospital of Santiago (CHUS/SERGAS), [7]Department of Oral and Maxillofacial Surgery, Complexo Hospitalario Universitario de A Coruña (CHUAC), [8]Department of Surgical Oncology, Instituto Português de Oncologia do Porto Francisco Gentil (IPO Porto), [9]Department of Medical Oncology & Clinical Oncology Group, Research Center (CI-IPOP), Portuguese Oncology Institute of Porto (IPO-Porto)/Porto Comprehensive Cancer Center Raquel Seruca (Porto.CCC), [10]Head and Neck Clinic, Instituto Português de Oncologia do Porto Francisco Gentil (IPO Porto), [11]Faculdade de Medicina Dentária da Universidade do Porto (FMDUP), [12]Department of Pathology, Portuguese Oncology Institute of Porto (IPO Porto), [13]Head and Neck Clinic, Instituto Português de Oncologia do Porto Francisco Gentil (IPO Porto), [13]Department of Pathology and Molecular Immunology, ICBAS-School of Medicine and Biomedical Sciences, University of Porto, [14]Translational Medical Oncology Group (ONCOMET), Health Research Institute of Santiago (IDIS), Complexo Hospitalario Universitario de Santiago de Compostela (CHUS, SERGAS)

Objective: To develop a saliva-based DNA methylation signature for the early detection of OC.

Methods: Genome-wide discovery of DNA methylation markers was performed on DNA extracted from tissue (tumor and adjacent non-tumor mucosa) and saliva samples from 19 OC patients, as well as saliva from 15 healthy controls, using the Infinium Human Methylation 850K BeadChip. Following bioinformatic analysis, candidate promoter hypermethylation markers were selected for further validation by quantitative methylation-specific PCR (qMSP) in a large multicenter cohort of saliva samples, including 157 oral cancer patients, 28 individuals with oral potentially malignant disorders, and 112 healthy controls. The diagnostic performance of individual and combined DNA methylation markers was assessed using receiver operating characteristic (ROC) curve analysis.

Results: In the discovery phase, focusing on gene promoter regions, we identified 2,752 differentially methylated CpGs (DMCpGs) between tumor and adjacent non-tumor tissues, and 12,984 DMCpGs in tumor versus normal saliva. In the validation phase, significant promoter hypermethylation of seven genes was detected in saliva samples from OC patients compared with healthy controls ($p < 0.0001$), with individual AUROC values greater than 0.80. The combination of two hypermethylated CpGs yielded the best diagnostic performance for distinguishing OC (accuracy 88.85%, sensitivity 89.17%, specificity 88.39%) and early OC (accuracy 88.62%, sensitivity 87.27%, specificity 89.29%) from healthy controls. In addition, this two-gene methylation panel discriminated oral epithelial dysplasia/OC from non-disease oral conditions with an accuracy of 87.21%, sensitivity of 87.95%, and specificity of 86.26%.

Conclusion: We developed a novel, sensitive, saliva-based DNA methylation diagnostic assay as a promising tool for non-invasive screening and early detection of OC.

O010

Risk factors and oncological impact of postoperative complications after total laryngectomy

Dr. Mariana Caetano[1], Dr. Carolina Arede[1], Dr. Cláudia Rosa[1], Dr. Paulo Pereira[1], Dr. Mafalda Oliveira[1], Dr. Ana Rita Santos[1], Dr. Diogo Tomé[1], Prof. Leonel Luís[1]
[1]ULS Santa Maria

Objectives: To analyze the incidence of postoperative complications after total laryngectomy, identify associated risk factors, and assess their impact on oncological outcomes.
Methods: We retrospectively reviewed consecutive patients undergoing total laryngectomy for laryngeal squamous cell carcinoma at a tertiary referral center (2014–2024). Demographic, pathological, and treatment variables were analyzed in relation to postoperative complications, with special focus on pharyngocutaneous fistula. Associations with adjuvant therapy compliance, recurrence, and survival were also assessed.
Results: Postoperative complications occurred in 34.4% of patients. The most frequent was pharyngocutaneous fistula (26.7%), followed by surgical site infection (4.4%) and lower respiratory tract infection (3.3%). On univariable analysis, prior radiotherapy, close or positive surgical margins, and lymphovascular invasion were associated with increased risk of fistula ($p=0.065$, $p=0.080$, and $p=0.024$, respectively). In multivariable analysis, prior radiotherapy remained an independent predictor (adjusted OR 3.59; 95% CI 1.11–11.61; $p=0.033$). Pharyngocutaneous fistula was not significantly associated with completion of planned adjuvant radiotherapy or chemoradiotherapy (81.8% vs. 85.7%; $p=0.73$). However, it was associated with increased risk of local or distant recurrence (42.3% vs. 24.6%; $p=0.049$) and significantly worse overall survival (5-year OS 28.3% vs. 46.7%; log-rank $p=0.038$).
Conclusions: Pharyngocutaneous fistula continues to represent a major postoperative challenge after total laryngectomy, particularly in patients with prior radiotherapy. Beyond prolonging recovery, its occurrence carries significant oncological implications, being associated with higher recurrence rates and worse overall survival. These findings emphasize the need for tailored perioperative strategies and close follow-up in high-risk patients.

O011

Prognostic Value of Depth of Invasion in Oral Cavity Squamous Cell Carcinoma of 4 cm or Less

Dr Jinho Kim[1], Dr Jun Yeong Song[1], Dr Joo Ho Lee[1], Dr Hong-Gyun Wu[1], Dr Keun Yong Eom[2], Dr Chan Woo Wee[3]
[1]Seoul National University Hospital, [2]Seoul National University Bundang Hospital, [3]Seoul Metropolitan Government Seoul National University Boramae Medical Center
Objective: We aimed to evaluate the role of the depth of invasion (DOI) as an independent prognostic factor in the absence of other adverse features in squamous cell carcinoma (SqCC) of the oral cavity with a size of 4 cm or less.
Methods: We performed a retrospective analysis in a multi-institutional cohort of patients with oral cavity SqCC, size of 4 cm or less. We included those who were treated with upfront surgery with negative resection margins from 2010 to 2021 and those with one or no nodal metastasis. Those who were treated with postoperative radiotherapy were excluded. The DOI and other adverse features, such as close resection margins, lymphovascular invasion, perineural invasion, and nodal metastasis, were evaluated in univariate and multivariate analyses for their association with locoregional recurrence (LRR).
Results: A total of 155 patients were included with a median follow-up of 23.7 months. 56 patients (36.1%) had DOI greater than 5 mm. 26 patients (16.8%) experienced LRR and one experienced distant metastasis. Multivariate analysis showed that DOI was the only prognostic factor associated with a higher rate of LRF ($p = 0.004$). The 2-year LRF rates of those with DOI ≤ 5 mm and DOI > 5mm were 4.7% and 30.3%, respectively.
Conclusion: This study implies that DOI greater than 5 mm may be an independent prognostic factor of the SqCC of the OCC and may be indicated for adjuvant radiotherapy.