Abstracts
Podium: Head and Neck Surgery 2
Monday, June 8, 2015 @15:30-16:00

Did the Addition of Chemotherapy to Radiotherapy Improve Survival in an HPV Negative Patient Population? – S. Hall, Kingston, ON

Learning Objectives

1. The attendee will learn that administrative data can be used to assess treatments and outcomes at the population level
2. The attendee will understand the change in incidence and treatment of hypopharymx cancer over time
3. The attended will realize that contrary to current beliefs the addition of chemotherapy made no difference to survival for an HPV –ve cohort

Background: The addition of chemotherapy to radiotherapy transformed the management of squamous cell head and neck cancers in the mid-2000s. The evidence for change was based on clinical trials but the question around HPV association and treatment effectiveness is still not answered. This study examines the evolution of treatments and outcomes in a HPV negative patient cohort. **Method:** A population–based study of 1070 patients from Ontario with a new diagnosis of hypopharyngeal cancer between 1995 and 2012. Patients were identified in the Ontario Cancer Registry and linked to their demographics, treatments and outcomes at the Institute for Clinical Evaluative Sciences (ICES). The treatment profile for each successive year is compared to the 3 yr survival for the patients of that year. **Results:** The incidence has declined over time, treatment has evolved from surgery or radiotherapy to chemoradiotherapy and there has been no change in outcome. **Conclusion:** The addition of chemotherapy to radiotherapy has not improved survival in an HPV negative patient population. Physicians, policy makers and funders need to consider the toxicity trade-offs when there is no demonstrable improvement in survival in real world practice.

High Throughput Screening for Drug Discovery in Head and Neck Squamous Cell Carcinoma – M. Black, N. Pinto, J. Yoo, D. MacNeil, K. Fung, London, ON, A. Datti, Toronto, ON, J. Barrett, A. Nichols, London, ON

Learning Objectives

1. To understand how high throughput drug screening can identify potent anti-cancer agents using genetically characterized cancer cell lines.
2. To uncover the genetic landscape of head and neck squamous cell carcinoma.
3. To understand how correlating genomic findings with drug response in head and neck cancer can lead to precision therapy in cancer.

INTRODUCTION Head and neck cancer outcomes continue to be poor despite advancements in chemotherapy, radiation therapy and surgery thus highlighting the need for novel therapies. OBJECTIVES To identify highly active drugs in head and neck squamous cell carcinoma (HNSCC) cell lines. METHODS High throughput robotic screening of 30 HNSCC cell lines, including 5 human papillomavirus (HPV)-positive lines, was carried out against 1585 compounds which included a large kinase inhibitor panel as well as known chemotherapeutics. Using a single dose of 4μM, data obtained from our screen was quantified in terms of B-scores, where a score less than 2SD below the mean of cellular proliferation was considered significant

and reported as a 'hit' for preliminary analysis of compounds effective at decreasing cell growth. Drugs with high activity were selected as hits and potency was confirmed with dose response curves. RESULTS The majority of hits demonstrated sub micromolar IC50 values in most of the HNSCC cell lines and could be grouped based upon their cellular target and/or function. These categories included: cytoskeleton disruption, transcription, protein modifications, as well as cell cycle regulation. Interestingly, novel targets such as stimulators of p53 function, inhibitors of the NF-κB pathway, and opiod receptors were also uncovered. CONCLUSIONS High throughput drug screening has identified a multitude of highly effective agents, many of which have never been previously tested in HNSCC. Antitumor activity needs to be verified in vivo in patient-derived xenografts before proceeding to clinical trials.

Transoral Laser Microsurgery for the Treatment of Primary and Recurrent Oropharyngeal Carcinoma – J. Melong, M. Rigby, M. Bullock, R. Hart, J. Trites, S.M. Taylor, Halifax, NS

1. Describe transoral laser microsurgery (TLM) as a surgical approach for the management of oropharyngeal carcinomas.
2. Review advantages of TLM over current management strategies and review current available evidence for its use.
3. Present efficacy and safety data on TLM for the treatment of oropharyngeal carcinoma at our center.

Background Transoral laser microsurgery (TLM) is a minimally invasive endoscopic surgical technique for the management of oropharyngeal and laryngeal carcinomas. It offers potential advantages over current treatment strategies including shorter recovery time, fewer complications and better functional outcomes, making it an appealing treatment option. Objective To assess the efficacy and safety of TLM for the treatment of oropharyngeal carcinoma. Methods All patients with oropharyngeal carcinoma undergoing TLM at our center were identified within a prospective database monitoring TLM outcomes. Kaplan-Meier survival analysis was used to evaluate the following end points at 24 months: disease-specific survival (DSS), disease-free survival (DFS) and local control (LC). Safety endpoints included complications following surgery and long term morbidity related to TLM. Results Between 2003 and 2014, 39 patients with oropharyngeal carcinoma underwent TLM resection. 28 (72%) patients had primary carcinoma, 9 (23%) were radiation/chemoradiation (RT/CRT) failures, and 2 (5%) had second primaries following previous RT/CRT. 3 patients had stage I disease, 8 stage II, 5 stage III, and 23 stage IV. HPV positive carcinomas were identified in 60% of patients. Kaplan-Meier estimates of 24-month DSS, DFS and LC for primary oropharyngeal carcinomas were 85.7% (SE 13.2%), 77.7% (SE 12.5%) and 85.5% (SE 10.6%) respectively. 24-month outcomes for RT/CRT failures were 55.6% (SE 16.6%) for DSS and DFS and 66.76% (SE 15.7%) for LC. 4 patients developed complications following surgery. Conclusions Observed 24-month efficacy and safety outcomes support the use of TLM for the treatment of oropharyngeal carcinoma.

Frequency of HPV16 Prevalence and PIK3CA Hot Spot Mutations in Early-stage Laryngeal Squamous Cell Carcinoma – M. Black, N. Pinto, J. Yoo, D. MacNeil, K. Fung, J. Barrett, A. Nichols, London, ON

1. To use real-time PCR to determine the HPV status and mutational profile of key hot-spot mutations in early-stage laryngeal cancer.
2. To identify predictive biomarkers for treatment-resistant early-stage laryngeal cancer by correlating mutational status with treatment outcomes.

INTRODUCTION Early-stage laryngeal squamous cell carcinoma is typically treated with radiotherapy or surgery. Although cure rates are often high, patients that fail radiation typically require a total laryngectomy. Biomarkers that could predict radioresistance could be extremely useful in optimizing treatment for laryngeal cancer patients. OBJECTIVES To determine the frequency of HRAS and PIK3CA hotspot mutations as well as human papillomavirus (HPV) status in early laryngeal cancer and explore their roles as biomarkers of radiation failure. METHODS Our retrospective patient cohort was comprised of 75 patients with early stage (T1-T2) glottis squamous cell carcinoma that were treated with radiation therapy at the London Health Sciences Centre. DNA was extracted from the patient samples and real-time PCR (RT-PCR) was used to identify hotspot mutations in PIK3CA as well as presence of HPV type 16 (HPV-16) to correlate biomarker presence with disease-free survival. RESULTS HPV-16 frequency in early-stage laryngeal cancer was found to be low (3/75=4%) and although not statistically correlated with outcome, all three patients were successfully treated with radiation. The only PIK3CA codon that was mutated in our cohort was H1047R (9/75=12%). PIK3CA mutation was not correlated with recurrence free survival. Results for HRAS mutation status are pending. CONCLUSIONS The prevalence of HPV-16 in early laryngeal cancer is low (4%) while PIK3CA mutations are more common (12%) in early-stage laryngeal squamous cell carcinoma. Although HPV-16 status and PIK3CA mutations were not found to be predictive of radiation failure, HRAS mutations may prove to be an important biomarker in this patient population.

Loop-Mediated Isothermal Amplification (LAMP): Detection and Sub-typing of Human Papillomavirus (HPV) in Oropharyngeal Squamous Cell Carcinoma – D. Livingstone, Calgary, AB, M. Rohatensky, Edmonton, AB, P. Mintchev, S. Nakoneshny, D. Demetrick, G. Van Marie, J. Dort, Calgary, AB

1. To establish the importance of HPV infection in OPSCC
2. To reinforce the need for a rapid, accurate bedside diagnostic test for HPV
3. To show the utility and potential of LAMP as a molecular diagnostic test

Background The incidence of oropharyngeal squamous cell carcinoma (OPSCC) continues to rise despite a decline in traditional risk factors. Epidemiologic studies implicate HPV as the likely etiology. Polymerase Chain Reaction (PCR), the current gold standard for assessing HPV positivity, is expensive, time-consuming and labour intensive. A simple, rapid and cost-effective method for detection and sub-typing of HPV is needed. Loop mediated isothermal amplification (LAMP) is a molecular diagnostic technique with comparable sensitivity and specificity to PCR. Our aim is to validate LAMP as a potential assay for subtyping of HPV in OPSCC. **Methods** Plasmids containing HPV 16 and 18 genomic DNA were obtained. Subtype specific LAMP primers were synthesized and the LAMP assay was optimized. HPV positive control plasmids were then serially diluted to establish the copy number detection threshold of the assay. Successful amplification was confirmed using visualization of precipitation formation, gel electrophoresis and turbidometry. **Results** HPV 16 and 18 LAMP reactions were successfully performed on HPV genomic DNA with subtype specific amplification without cross reactivity of the primers. Detection thresholds for HPV 16 and 18 were found to be 10^5 copies and 10^3 copies, respectively. Amplification products were consistently confirmed across all detection methods. **Conclusions** This study demonstrates the feasibility of utilizing LAMP for the detection and subtyping of HPV in OPSCC. The LAMP reactions were sub-type specific, with a detection threshold comparable to PCR. The assay holds great promise as a bedside diagnostic technique that can deliver vital prognostic information with potential therapeutic implications.

Predictors of Failed and Delayed Decannulation After Head and Neck Surgery: A Case-Control Study – S. Anderson, A. Isaac, C. Jeffery, J. Robinson, C. Korownyk, V. Biron, H. Seikaly, Edmonton, AB

Learning Objectives

1. Discuss the rationale for temporary tracheostomy at the time of head and neck cancer resection (HNC-R).
2. Describe the morbidity and complications associated with failed and delayed decannulation.
3. List the variables associated with failed and delayed decannulation in HNC-R patients.
4. Discuss strategies for modifying risk factors and counselling patients regarding risk of persistent tracheostomy after HNC-R.

Objective: To determine the variables that are predictive of failed and delayed decannulation in patients who underwent head and neck cancer resection (HNC-R) with tracheostomy. **Design:** Retrospective case-control study **Methods:** All patients who underwent HNC-R with immediate free tissue transfer reconstruction and tracheostomy who had failed or delayed decannulation between 2011 and June 2014 were included. Failed decannulation was defined as persistent tracheostomy at the time of discharge, or persistent tracheostomy at 60 days post-surgery. Delayed decannulation was defined as persistent tracheostomy at 10 days post-surgery. Controls were matched for age, sex, time of surgery, surgeon, and TNM stage. Odds ratios for risk of failed decannulation were calculated for each variable. Multivariable Cox Regression Analysis was used to determine predictors of days to decannulation. **Results:** 18 consecutive patients with failed decannulation and 41 patients with delayed decannulation were included, along with 59 matched controls. Total glossectomy (OR=56.3 [8.4-180.1]), total base of tongue resection (OR=32.0 [3.4-99.9]), anterolateral thigh flap reconstruction (OR=2.1 [1.3-9.6]), smoking at time of surgery (OR=4.2 [1.4-12.7]), and pack years (OR=1.06 [1.02-1.11]) were associated with failed decannulation. Cox Regression Analysis showed that total glossectomy (Exp(B)=7.1 [2.1-24.6]), and smoking status (Exp(B)=5.0 [1.7-14.1]) were independent predictors of days to decannulation. **Conclusions:** Patients with total glossectomy defects after HNC-R, and those that continue to smoke to the time of surgery are at increased risk for delayed and failed decannulation. Patients should be appropriately counseled about these risks, and effort should be made to address the modifiable risk factors.